REPORT TO THE PROVINCES AND TERRITORIES

Genetics, Testing & Gene Patenting:

Charting New Territory in Healthcare

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INTRODUCTION

The multitude of recent and anticipated research developments in the fields of genetic information and genetic technologies hold out the potential to fundamentally re-define medicine within the lifetime of many Canadians.

Even as jurisdictions collectively focus attention on how best to manage healthcare today, we must also retain our focus on the future, on addressing how we modernize and renew. Sustaining healthcare must also be about retaining and strengthening our capacity to innovate and lead. In this regard, the research breakthroughs in human genetics will come to play an increasingly important role, a role, which if appropriately managed, promises much for both healthcare and society in general.

This future role is one for which our jurisdictions can and must take bold steps, in the present, to begin to prepare. In anticipating and attempting to chart the course that genetics will take healthcare and society, Canada would not be alone.

Jurisdictions around the world are currently working to understand and address the social, legal, ethical and policy challenges presented by new genetic breakthroughs.

Canadian researchers have already played significant roles in the international efforts to decode the human genome and bring forward new interventions in the field of medical genetics. So too, in the Canadian biotechnology sector, major breakthroughs are being pursued.

It is estimated that 60% of Canadians will experience a disease with some form of genetic component during their lifetime. Genetic technologies hold out the potential to help a large majority of Canadians.

Governments, at both the federal and provincial/territorial levels, must now match the determination and success of the efforts in science with an equal resolve to begin to understand and address the ethical, legal, social and health-system implications of new developments in genetics. Canada must not lose any more time in putting in place appropriate frameworks to assist both healthcare and society in general to adequately prepare for the changes ahead. As the Saskatchewan Health Services Utilization and Research Commission rightly noted:

> " We have a window of opportunity in which to act while things are still in a manageable scale. By working now to establish the necessary policies and institute the required changes in the health system, we can ensure that the inevitable growth in genetic testing proceeds in accordance with scientific evidence and in a way that enables us to reap its full potential."[1]

This is sound advice, which concurs with the expert opinion that has been provided in Ontario by the Ontario Advisory Committee on New Predictive Genetic Technologies.

For while there is much hope, new breakthroughs in genetics also carry many risks.

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[1] *Saskatchewan Health Services Utilization and Research Commission. HSURC Brief. Staying ahead of the wave: Preparing for today for genetic testing tomorrow. October 2001. www.hsurc.sk.ca*

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HIGHLIGHTS

This report details a range of areas for possible action, on which jurisdictions might choose to act in concert to better prepare both healthcare and society for the impact of genetics. These are:

INTERJURISDICTIONAL FRAMEWORK:

This report is a call for the development of a shared vision across jurisdictions and for the development of shared resources. In short, it is a call for a comprehensive, patient-centred framework to assist jurisdictions in maximizing the benefits offered by new technologies and to set paths for collaborative work to better understand and address the risks.

A comprehensive framework, if developed, could help move Canada and all provinces and territories into the forefront of preparing for the impact of genetics. This preparation will need to take several forms. There is a strong need for greater public engagement, for increased capacity in our health system to incorporate change, and for examining new ways in which we regulate and protect.

PUBLIC EDUCATION AND ENGAGEMENT:

The report outlines the growing need for public engagement and education on matters concerning genetics in healthcare. The report suggests a range of steps to better prepare. These might include reviewing existing school curricula, increasing coordination and intensity of public education activities in genetics and developing multi-sectoral approaches to ensure that accurate and credible information is made available.

PROFESSIONAL EDUCATION:

The report notes the need for increasing training in medical genetics for a range of healthcare providers as an essential preparatory step to meeting the challenges of incorporating new technologies. The report suggests cross-jurisdictional coordination and partnerships with appropriate professional associations to advance health professional education.

GENETIC TECHNOLOGY ASSESSMENT:

The report notes the rising rate of commercial development in genetics and the need for all jurisdictions to have access to high quality, objective health technology assessment and health economic analysis in the genetics field. The report proposes new capacity be added making this information available to all jurisdictions.

SERVICE DELIVERY: QUALITY CONTROL:

The report notes that additional standards and review processes may be required to deal with new testing methodologies and approaches. It is suggested that building on existing capacity and expertise, a framework for quality control be developed for jurisdictions to use where possible, to avoid duplication and divergent standards. The issue of kit and home-based testing through direct-to-consumer advertising is examined and the federal government is called on to examine the existing review process and develop information sharing capacity regarding these developments.

SERVICE DELIVERY: HUMAN RESOURCES:

Noting the potentially significant increases in genetic testing coming in the near term, the report states that jurisdictions will require improved capabilities to track and project future needs. Given international competition that will exist in the area of human genetics, the report suggests coordinated approaches to health human resource planning in this field.

PRIVACY, DISABILITY AND DISCRIMINATION:

Ensuring the appropriate involvement of the disabled community in decision-making regarding genetic testing and research is presented as an important factor in helping society negotiate the boundaries of ethical treatment. The report also notes growing concern with regard to potential uses of genetic information and proposes jurisdictions work to put in place appropriate protections particularly in the areas of insurance and employment.

PATENT REFORM:

The report notes the recent call by the federal Standing Committee on Health for a complete ban on gene patents. Recognizing the role of the biotechnology sector in promoting innovation, the report does not support a ban, but instead calls for a comprehensive review of the federal *Patent Act* providing a range of concrete proposals such as the introduction of an opposition period, additional infringement protection for healthcare providers, tightening utility requirements and restricting broad-based patents.

OVERSIGHT AND REGULATION: INTERJURISDICTIONAL CO-ORDINATING BODY:

The report urges governments to work together to ensure appropriate and comparable quality standards are in place across all jurisdictions providing genetic testing including; appropriate criteria for deciding when to test, monitoring processes for lab quality, protocols for ensuring appropriate counseling and support, and processes regarding test reviews for accuracy and reliability.

The report notes the need for appropriate capacity to monitor trends in medical genetics and assist all jurisdictions in addressing the ethical, legal and service delivery issues they will face. Stressing the need for a coordinated approach, the report suggests the possible creation of a human genetics commission to assist all jurisdictions.

The report also notes the importance of ensuring comparable quality assurance regimes and standards are in place and urges jurisdictions to cooperate in developing common approaches. In terms of federal review and approval processes, the report stresses the need for vigilance in the review and approval of new kit-based forms of genetic tests.

CO-ORDINATED AVAILABILITY OF TESTING:

Noting the increasing number of tests that will be available and the importance of attempting to develop fair access, the report suggests that jurisdictions examine the creation of protocols to help ensure access to testing for all residents. The report notes that with cooperation and good planning, the range of tests (especially for low-volume, rarer conditions), could be improved by coordinated cross-jurisdictional delivery.

SUPPORT FOR BIOTECH SECTOR:

The report notes the valuable contribution of the biotechnology sector to economic growth and healthcare innovation and suggests that innovative measures taken in the United Kingdom (UK) and the United States of America (USA) to spur biotechnology development may warrant study by jurisdictions.

THE POTENTIAL IMPACT ON COSTS:

The report notes that the growth in genetic-based medicine will necessitate many changes in healthcare and delivery at the individual and system level and that these changes will be associated with costs. The report notes that estimating the economic impacts of genetic technologies is complex and far from straightforward. The cost implications of the test itself is only one component of overall system costs and in many cases is minor compared to the cost for surveillance, prevention and treatment. The report notes that wise policy choices can ensure that savings, where available, are realized, and where cost increases come into play, the most value is obtained for the resources devoted to genetic testing.

THE ROAD AHEAD

By putting in place the components of this framework, the appropriate protections and review mechanisms, by increasing educational efforts and preparing we can begin to achieve two very important goals.

Firstly, we can equip all participants in the healthcare system with the tools and knowledge which will increasingly be required to navigate what will become more complex terrain in various fields.

Secondly, we have the opportunity to build a climate in society where the general understanding and acceptance of genetic innovation is increasingly shaped by reasoned consideration and a balance between the public and private good.

Such a process is, no doubt, a potentially difficult one. It is complex terrain and there are strongly divergent interests. That said, Canadians need to know that action is being taken, that jurisdictions will not simply adopt a wait and see approach. They need to see that opportunities and challenges are being taken seriously and that we are working collectively to address them and prepare for the future.

If sustaining healthcare means, as it must, maintaining and increasing our capacity to integrate new technologies and offering to Canadians the most appropriate and advanced healthcare that we can, then there is an urgent need for the healthcare system to have access to the necessary resources to adapt. The report underlines the need for federal action on a range of fronts, not the least of which must be ensuring that our healthcare system is adequately resourced to keep pace with the benefits of medical science as it continues to evolve.

At the August 2001 Premiers conference in Victoria, Ontario committed to produce a report for Premiers on genetic patenting and the growing importance of genetic medicine for healthcare. This report is an attempt to canvass the critical factors at play and highlight possible viable approaches for jurisdictions to collectively advance.

During development of the steps required to implement a viable framework, traditional notions of health and healthcare will need to be examined, such as the potential of health care to gradually evolve from a schema informed primarily by 'diagnose and treat' to a 'detect and manage' paradigm. A framework will also need to balance the 'right to know' and the 'right not to know' and engage public perceptions of genetic tests as 'definitive proof' of having a condition versus the complex interplay between genes, lifestyle and the environment. Ultimately the major question will be how we balance individual benefit from emerging technologies with public affordability.

KEY THEMES

INTERJURISDICTIONAL FRAMEWORK

The framework called for in this report is not meant to be a rigidly prescriptive one. It merely offers jurisdictions some markers – possible approaches that provinces, territories and the federal government might choose to take collectively to strengthen our capacity to understand, incorporate and respond to the breakthroughs in genetic technology, while still maintaining the appropriate levers and supports at the provincial and territorial level. The report therefore sets out a series of possible actions for consideration and calls for further collaborative work on the part of governments, providers, educators, patients and industry.

PUBLIC EDUCATION AND ENGAGEMENT

Citing both Canadian and International data, the report suggests that potentially major demand and strong interest exists among the Canadian public for new genetic technologies. This interest is however matched by individuals having a strong sense of not being informed about progress in genetics and related implications (89% of Ontarians polled in 2001 were very or somewhat interested in genetics while 71% indicated however that they felt they knew only a little or nothing at all).

This report notes that without a stronger capacity to engage the public in issues surrounding genetics, there is a high degree of risk that patients may, in the future, be ill-equipped to adequately assess the options available and thereby navigate, with confidence through potentially difficult and complex choices. In particular, circumstances will arise where treatments for conditions are simply not yet available, or where there are complex interactions between genetic predisposition, lifestyle and environment requiring the consumer to make well-informed choices and decisions.

In society at large, without greater public awareness it will also be more challenging for the biotech sector to build the confidence and awareness necessary for a greater, more informed acceptance of the positive contributions that biotechnology can make to Canadian society.

This report notes the role of Genome Canada in promoting education and calls for Industry and Health Ministers to work collaboratively with colleagues on a coordinated strategy for public education across jurisdictions recognizing this as a multisectoral task.

PROFESSIONAL EDUCATION

A knowledge of genetics and the psychosocial aspects of care and treatment will become increasingly important for a broad range of healthcare workers including family physicians, nurses, pharmacists and non-genetic medical specialists. The report calls for jurisdictions to establish a common approach to increasing the training opportunities available at various levels for healthcare professionals in the field of genetics, involving professional associations, industry, educational institutions and bodies such as Human Genome Canada.

The report suggests that this education is an essential preparation for the future and should be coordinated between jurisdictions to ensure greater consistency and to avoid jurisdictions overlapping and duplicating individual efforts.

GENETIC TECHNOLOGY ASSESSMENT

High levels of public interest in new genetic breakthroughs, combined with the rapid commercialization of genetic knowledge will undoubtedly mean that publicly funded health systems will increasingly be required to evaluate claims and counter-claims regarding new genetic technologies and new approaches to treatment.

For all jurisdictions, the capacity to incorporate new genetic technologies in a responsible and effective manner will require improving our collective capacity to assess, evaluate and monitor the relative effectiveness and cost-impact of new genetic technologies relative to existing treatments and procedures.

Without strengthened capacity, there is real risk that misleading, commercial marketing entering Canada from other jurisdictions and via the Internet, combined with the risk of possible premature commercialization could all play a very strong role in influencing the types of tests and interventions which are available or indeed which become publicly funded.

Building on the progress provinces and territories are making in more collaborative pharmaceutical assessment, the report calls for the creation of a new and strengthened capacity for genetic technology assessment, including the potential for the creation of a new agency with specialized capacity to provide all jurisdictions with reliable, timely and objective analysis of new genetic technologies.

The report notes the need to build upon the existing capacity scattered across a number of jurisdictions and the great advantage of avoiding duplication between jurisdictions.

SERVICE DELIVERY: QUALITY CONTROL

There is a need for additional mechanisms and regulations for genetic technologies in order to effectively monitor the quality of services provided. Governments should strive to put in place protections and appropriate testing protocols that jurisdictions need to develop and maintain. As new testing methodologies develop, mechanisms will be required to effectively monitor quality areas such as:

- Testing criteria (under what guidelines and to whom should the test be offered?)
- The accuracy and reliability of the test (should the test be offered?)
- The relative benefit of a new test
- The accuracy and reliability of laboratories conducting the test
- Training of test personnel (are they qualified to perform their duties correctly?)
- The testing process (are patients giving informed consent?)
- The availability or anticipated availability of appropriate treatments or interventions.
- The degree to which patients are receiving a full package of services (are patients receiving adequate pre- and post-test counselling?)

The report notes that Canadians and our healthcare system will be impacted by the possible rise in at-home tests and the availability of such tests over the internet. It is suggested that federal standards for approval for review of such at- home tests be carefully examined and monitored to ensure that they adequately protect Canadians. It is suggested that direct to consumer marketing of genetic testing should be clearly circumscribed if not entirely prohibited for certain forms of testing.

SERVICE DELIVERY: HUMAN RESOURCES

All jurisdictions have faced the significant challenge of ensuring an adequate supply and distribution of physicians, nurses and other health professionals in the midst of an international shortage in many of these professions.

With the anticipated rate of growth of genetic testing we must also face the challenge of beginning to plan now for our human resource needs of the future. Genetics is an international field, highly specialized and qualified, knowledgeable personnel are highly sought after. Geneticists, trained genetic laboratory personnel and genetic counsellors are some of the specialists that are required in delivering services. Genetic counselling to assist patients in making difficult determinations about their care and treatment will unquestionably be a field of increasing importance. All of these specialties are already in relative short supply in jurisdictions currently providing genetic testing.

This report calls for jurisdictions to put in place a shared plan for increasing our capacity to project future needs and to develop a cross-jurisdictional framework to assist jurisdictions in obtaining the appropriate supply and distribution of the skilled personnel that will increasingly be required as healthcare evolves while retaining the valuable expertise that already exists in many jurisdictions. The report notes major investments in genetic expansion that have already been made by jurisdictions such as the United Kingdom and suggests that such advance planning must also be undertaken in Canada.

PRIVACY, DISABILITY AND DISCRIMINATION

Personal health information is some of the most sensitive information about an individual that there is. Genetic information is an obviously important component of personal health information, however, it is a form of information which also raises some unique fears and concerns. Genetic tests reveal information not only about the individual but about families. Technology will allow hundreds of tests to be carried out simultaneously using a drop of blood or hair sample. The capacity to scan hundreds of thousands of samples in minutes will make large-scale screening quite simple. Large databases of genetic information can be created, some of which may exist outside Canada.

The report notes the high levels of concern that exist regarding the possible uses of genetic information by employers and the parallel questions that many Canadians have about how genetic information might be used by insurers. Likewise Canadians need to be assured that data linking and the secondary uses of genetic information are appropriately controlled.

The report outlines the potential for these types of concerns to create a climate which impedes the use of genetic testing in healthcare and therefore the report underlines the need for jurisdictions to take the necessary steps to ensure that appropriate protections are in place.

Many states in the U.S. and across Europe have already taken important steps to put in place specific protections, either legislative or negotiated, to protect the privacy of genetic information and prevent its misuse. Some U.S. law specifies that genetic predisposition will not be considered a pre-existing condition for group health insurance plans. Innovative steps have been taken in the UK to develop voluntary moratoriums on the collection of most forms of genetic information by insurers. Canada, perhaps, has not kept pace.

Similarly, policy principles put forth by the U.K. Human Genetics Commission propose that employees not be required to take genetic tests for employment and that genetic test results should only be used if needed to assess current ability to perform a job safely or assess susceptibility to harm.

The report therefore proposes that Canadian jurisdictions develop common or consistent principles to govern the use of genetic information in employment and insurance and proceed to take steps to appropriately enshrine these protections.

Legislative and policy initiatives are required to protect the interests of children with respect to genetic testing.

Furthermore, genetic breakthroughs carry with them the often exaggerated promise of eliminating certain diseases or conditions. In assessing this promise, the report states that serious consideration must be given to the ethical boundaries of treatment. It is clear that gene technology should be used to assist people rather than to eliminate diversity.

This report stresses the need for the involvement of people living with disabilities and genetic conditions in the discussion of the boundaries of treatment.

PATENT REFORM

Citing the extensive international debate around the practice of the patenting of human genes and DNA, the report examines some of the unique challenges that gene patenting might create. The report recognizes the role of the biotechnology sector in the Canadian economy, the international agreements to which Canada is a party and the important contributions made by the biotech sector to healthcare innovation.

In attempting to think through the potential solutions available to both some of the practical and systemic concerns that exist, this report suggests returning to the fundamental concept of the patent as a contract between society and the inventor. In this regard, while recognizing the important role patents play in protecting innovation, the report suggests that society must also have a role in determining the terms of that contract.

The report notes that there are three main directions Canada can choose to take.

The first approach is that which has been recommended by the Federal Standing Committee on Health. In December 2001, this committee called for a complete ban on gene patenting.

The second is to simply retain the status quo. As Canada already lacks a number of protective measures that exist in other jurisdictions, standing still, may, in effect, amount to simply falling behind, both from the perspective of the biotechnology sector and in terms of meeting the concerns of the public at large.

The third approach called for in the report is the more complex and more challenging but ultimately a more appropriate route to take. Acknowledging the work of the Canadian Biotechnology Advisory Committee and drawing on recent experience in the European community, the report calls for the undertaking of a rigorous review of how and in what form patents should be granted on human genetic material and presents a range of options for putting in place more appropriate balances and protections. This would include an examination of issues associated with stem cell and sub-gene patents.

In Canada, the *Patent Act* is under federal jurisdiction. Working with provinces, territories, industry, consumers and other interested stakeholders, the federal government should review the *Patent Act* and the associated processes and supports involved in the patent procedure. In undertaking this review, the federal government should consider the following approaches:

CLEAR PROTECTION FOR RESEARCH AND CLINICAL NON-COMMERCIAL USE

The report notes the need for clear and unambiguous protection from patent infringement liability for healthcare providers and researchers working on genetic materials, which may be patented. The report also notes existing research exclusions in the *Patent Act* but notes the need to strengthen this approach in order to ensure that individuals whose research work may eventually have a commercial application are not effectively blocked by patent from pursuing improved techniques.

IMPLEMENTING CLEAR AND MODERN STANDARDS

The report notes the extensive work undertaken by the U.S. Patent Office to increase utility standards, provide training and interpretive manuals to staff on gene patents and suggests that this step is overdue in Canada. The report also notes that training and interpretive resources are required by both industry and the public as a clear guide to the practices and criteria employed. The report urges immediate action in this regard.

CLARIFY DEFINITION OF PATENTABLE SUBJECT MATTER

Noting that a patent on a gene is unique in that in certain cases genetic materials can be found to have multiple uses in different combinations, the report suggests that the patenting of "concepts" or general, non-specific utilities, is highly problematic and could potentially result in a direct or indirect block to research and development. The report suggests the need for narrowing the subject matter for which genetic material can be patented including the identification of specific uses and the examination of sub-gene and stem cell patents.

METHODS OF MEDICAL TREATMENT

The report cites the fact that methods of medical treatment (e.g. new surgical techniques) are not patentable in Canada and suggests that this exclusion be extended to the use of genetic materials in diagnosis. Different diagnostic technologies themselves would still under this approach be patentable, but the simple use of patented genetic materials in diagnosis per se would not expose a clinician to liability.

ORDRE PUBLIC/ MORALITY

The report notes the presence of an ordre public/morality provision in the patent legislation of a number of countries and its inclusion in the European Directive on Legal Protections for Biotechnology. The report draws upon recent research breakthroughs in stem cell research and human cloning and illustrates that patents in many areas of stem cell manipulation have already been sought. The report therefore suggests that the inclusion of a comparable ordre public/morality provision in Canadian patent law may be a valuable tool to limit patents on processes or procedures, which are deemed contrary to Canadian morality or ethics.

OPPOSITION PERIOD AND APPEALS COURT

The current practice of the European Patent Office is to have a nine month opposition period that can be utilized by individuals or agencies seeking to challenge the scope, content or validity of a newly granted genetic patent. The report also notes that this opposition process is not court based, is inexpensive and co-exists with a patent approval process significantly more expeditious than Canada's. The report notes the value of the opposition procedure in promoting transparency in the patent granting process and suggests the introduction of such a process in Canada be considered. A specialized court to handle the appeals of the Patent Office's decisions and to adjudicate in matters of gene patent validity and infringement should be considered.

COMPULSORY LICENSING

The Ministerial Conference of the World Trade Organization in Doha, Qatar in November, 2001 stated that nations should be able to take measures "to protect public health and in particular, to promote access to medicines for all." The Ministers also stated that countries have the right to determine the grounds upon which they grant compulsory licenses. This concept must include providing access to the diagnostic procedures necessary to determine when and which medicines to provide. The federal government should consider compulsory licensing of patents relating to the provision of genetic diagnostic and screening tests, granted by the Commissioner of Patents in return for a reasonable royalty fee.

The goal of any patent reforms should be to uphold the beneficial aspects of patent law (e.g. encouraging research, invention and innovation) while ensuring a better balance between private and public interests with appropriate transparency and rigour.

INTERJURISDICTIONAL CO-ORDINATING BODY

The greater incorporation of genetic technologies and the breakthroughs of genetic research into both healthcare and society will not be without significant challenges. This report suggests that the changes will not happen overnight, but sporadically and incrementally, leaving jurisdictions with the choice to either simply adopt a reactive role, moving from one challenge to another, in isolation, or to adopt a more co-ordinated forward-looking approach.

In making this assessment, the report examines models that have been adopted in other countries to examine the role of genetics in society and calls upon Canadian jurisdictions to consider the possible creation of a broad-based Human Genetics Commission with the responsibility to co-ordinate expertise from across jurisdictions and sectors and to assist all governments in better tracking and anticipating forthcoming healthcare advances.

Such a body might also be charged with assisting jurisdictions in monitoring the impact of genetic testing and treatments, examining the ethical and legal challenges that may arise unique to healthcare, and reviewing the implications for healthcare delivery from both a patient and system perspective. All provinces and territories would also benefit from the creation of a forum within which capacity can be shared across jurisdictions. This body might also potentially house much needed new capacity in genetic technology assessment which could be available to all jurisdictions.

CO-ORDINATED AVAILABILITY OF TESTING

Beyond the evaluation of emerging genetic technologies, owing to their highly specialized nature, the report suggests that provinces and territories begin to examine how best to more formally co-ordinate the delivery of certain forms of genetic testing.

In this case, the report envisages more formalized co-ordinated delivery systems for genetic testing which crosses jurisdictions. Increasing co-ordination would not only allow for greater specialization but would offer a rational approach to addressing rarer genetic conditions, for which the numbers of tests required may be too limited for one jurisdiction to justify putting in place the necessary capacity.

This process in the medium term could potentially allow for Canadians in all parts of the country to benefit from improved access to a broader range of tests at a lower cost than the gradual evolution of disconnected systems. The report suggests Health Ministers examine the availability of testing now and the protocols that might be required to build more co-ordinated systems.

SUPPORT FOR THE BIOTECH SECTOR

Canada's biotechnology sector is a vibrant contributor to the growth of the Canadian economy in terms of jobs, research and investment. The report outlines the capacity for Canada to continue its leadership in biotechnology and suggests approaches worthy of study by the federal government and other jurisdictions to help sustain and promote growth in the biotech sector. Approaches taken by other jurisdictions such as the United Kingdom and a number of U.S. states, including the promotion of research clusters and development zones require consideration for their greater application to biotechnology in Canada.

THE POTENTIAL IMPACT ON COSTS

The growth in genetic-based medicine will necessitate many changes in healthcare and delivery at the individual and system level. Further understanding of genetics will prompt the development of new diagnostic and treatment models. Such services may include population-based or individual screening for specific disorders, presymptomatic medical therapies and ways to meet the challenges of greater precision in diagnostic techniques. Understanding the psychological effects of this knowledge on individual health and appropriate counselling will also become an increasingly important component of medical care and treatment. Canadian healthcare systems will need to offer the possibility of earlier detection of disease and enable doctors to focus on prevention as well as treatment of disease through models developed from genetic discoveries.

The report clearly notes that short term demand for genetic testing will be extremely strong. Noting the increased utilization that has been seen of tests currently available and the considerable number of tests anticipated to become available, the short-to - medium term cost pressures will be potentially significant.

It is also the case that for many of the tests for which there will be strong public demand, predictive genetic tests, by and large the newer forms of testing, will not simply replace existing tests, but will often co-exist with existing tests. Unless carefully controlled, the availability of at-home kits could also indirectly have a major impact on costs for the publicly funded healthcare system.

As such, there is some risk that provinces and territories could see a wide range of new predictive genetic tests emerge for which the costs may be relatively high and the possible impact on health highly variable. While some testing will undoubtedly offer opportunities for more effective interventions and earlier treatment, the positive effects will likely take several years to be felt while the costs will need to be borne in the short-to-medium term. In many cases, the cost of the test itself will only be the 'tip of the iceberg'.

Separate from new genetic tests are the breakthroughs in pharmacogenetics which will see increasingly individualized treatments evolving based upon genotyping (using genetic information to understand the responsiveness of individuals to different forms of medication). This form of drug development has many positive aspects, not the least of which will be the possibility to reduce the high human and financial toll from adverse drug reactions. That said, the costs can be anticipated to be large in the short-to-medium term as the research and development investments that have gone into the creation of so called "smart-drugs" are high and industry will be looking to recoup costs.

Gene therapies, genetics, proteomics and DNA microchip technology also hold significant future promise as well as raising significant potential ethical and financial considerations. Again, the health economic benefits accruing from new and emerging technological contributions may prove to be extremely hard to realize in the short-to-medium term, while the short-to-medium term costs of providing access to these innovations will be high.

Strengthened training and staffing to ensure appropriate genetic expertise in the health system is essential if healthcare is to be equipped to rapidly and effectively incorporate new techniques. This training will require cross-jurisdictional coordination and financial support if it is to have the reach and impact required.

If sustaining healthcare means, as it must, maintaining and increasing our capacity to integrate new technologies and offering to Canadians the most appropriate and advanced healthcare that we can, then there is an urgent need for the healthcare system to have access to the necessary resources to adapt. The report underlines the need for federal action on a range of fronts, not the least of which must be ensuring that our healthcare system is adequately resourced to keep pace with the benefits of medical science as it continues to evolve.

CONCLUSION

The acceleration of genetic research over the past decade has opened up a new realm of possibilities for human health and wellness. Healthcare in Canada and around the world will eventually be transformed in many ways by the breakthroughs that even a decade ago few of us could have foreseen.

Governments have much to contribute to preparing society and preparing healthcare to be positioned to draw upon the best of genetic medicine while putting in place the necessary checks and balances which can assist in limiting the risks that undoubtedly come with this terrain.

Building on the tremendous progress that has been made by Canadian researchers in the decoding of the human genome, Canada must now set a goal of not simply housing groundbreaking science, but preparing society to appropriately harness such innovation.

This report has sought to provide a series of markers to assist all jurisdictions in coming to terms with their own unique challenges and issues in a manner which allows them to draw upon the experience and expertise of others.

We call on the federal government to play a critical role in supporting this process, in recognizing and acting upon areas of change which are required, but also to give full consideration to the enormity of some of the challenges that healthcare will face as we attempt to re-shape the skills, methods and tools required for the most advanced forms of medicine.

This report is intended to generate discussion and dialogue and to offer some suggested routes for us to take – in the end, the final product will be what jurisdictions choose to make it. The hard work lies ahead.

The full list of actions proposed in the report are set out below, more detail on each of the recommendations can, however, be found in the final section of the report.

RECOMMENDATIONS FOR POSSIBLE ACTIONS:

CROSS-JURISDICTIONAL FRAMEWORK

1. **Task Health Ministers in conjunction with appropriate colleagues to develop a comprehensive cross-jurisdictional framework on human genetics and healthcare. The framework should be patient-centred and take into consideration the social, legal, ethical, financial and health system implementation issues raised by the increasing role of genetic breakthroughs in healthcare.**

   The goal of a comprehensive framework would be to undertake in a co-ordinated manner a wide range of specific actions designed to maximize the ability of the Canadian health system to utilize the breakthroughs offered by new genetic research in an informed and forward looking manner.

   Such a framework should encompass:

   a) **Co-ordinated and intensified public engagement on the role of genetics in healthcare.**

   b) **Increased opportunities for the education and training of health professionals in genetics and new genetic medicine.**

   c) **Strengthened shared capacity in health technology assessment and health economic analysis for genetics.**

   d) **Developing appropriate shared quality control mechanisms (testing protocols, laboratory and test evaluation mechanisms, appropriate consumer protections).**

   e) **Developing common increased capacity in health human resource planning for genetics and putting in place a shared multi-year plan for genetic expertise in the health system.**

   f) **Developing the common principles to underpin privacy, disability and discrimination protections regarding the use of genetic information particularly in the employment and insurance fields.**

   g) **Examining comprehensive patent reform and reform to the patenting processes for human genetic materials.**

   h) **The establishment of a cross-jurisdictional co-ordinating body to provide assistance and expertise to all jurisdictions (Human Genetics Commission).**

   i) **Putting in place the basis for a co-ordinated shared delivery system for genetic testing across jurisdictions.**

   j) **Support for innovative biotechnology sector through continued examination of international best practices for supporting strength and growth in this sector.**

PUBLIC EDUCATION AND ENGAGEMENT

2. **Task Health and Industry/Economic Development Ministers in conjunction with other appropriate colleagues to participate in drawing up an interjurisdictional framework for public education in genetics and biotechnology for future consideration. Such a framework might examine contributions that could be made by a variety of sectors and existing agencies and determine the steps best taken to maximise information sharing and coordination.**

PROFESSIONAL EDUCATION

3. **Provincial and territorial Health Ministers through appropriate channels and drawing upon colleagues from other sectors as required could begin by undertaking a "census" of where we are now and from this point on, with federal cooperation and financial support and in conjunction with appropriate professional agencies, set out a series of key targets for improving the training and educational opportunities available to our healthcare workers. The goal would be to develop a multi-year framework for increasing these skills and training opportunities.**

GENETIC TECHNOLOGY ASSESSMENT

4. **Building on the progress being made by Health Ministers regarding collaborative pharmaceutical assessments, provincial and territorial Health Ministers could be tasked with establishing a workplan, objectives and timeframe for developing optimum current and future collaborative capacity in genetic technology and testing assessment and evaluation. Such a collaborative process should receive at least partial federal funding and be available to all jurisdictions. Assessment would include economic evidence relative to cost-benefit and medical efficacy studies being conducted both pre and post test approval.**

5. **Provinces and territories might also wish to task Health Ministers with examining the feasibility of "conditional approvals" on certain testing where sufficient evidence is not yet in place to allow a complete determination of the direct and indirect implications of test coverage.**

SERVICE DELIVERY: QUALITY CONTROL

6. **Health Ministers could be tasked with establishing a common framework for quality control in genetic testing to be utilized to the extent possible across all jurisdictions. Such a framework which could include testing criteria and standards, should build upon existing capacity and expertise and avoid, to the extent possible, duplication and divergent standards.**

7. **Provinces and territories could assess with Health Canada and Industry Canada existing review processes and develop an information sharing capacity regarding new developments in kit and at-home based testing in this regard.**

8. **Provinces and territories could also call on the federal government to ensure that direct to consumer marketing of genetic testing should at minimum be clearly circumscribed if not entirely prohibited for certain forms of testing.**

SERVICE DELIVERY: HUMAN RESOURCES

9. **Health Ministers could be tasked to use appropriate existing mechanisms such as the Advisory Committee on Health Human Resources (ACHHR), and where, appropriate drawing in Education Ministers to undertake a comprehensive review of existing and projected health human resource needs in the field of medical genetics. Health Ministers could be tasked to develop a medium range plan with the goal of providing an adequate and appropriately distributed supply of genetic expertise to residents of all jurisdictions.**

10. **Health Ministers might also be tasked with ensuring that ongoing independent capacity is in place to deliver independent quantitative analysis on supply, distribution and forecasted requirements of specialized skills in genetics (geneticists, laboratory expertise, counsellors).**

PRIVACY, DISCRIMINATION AND DISABILITY

11. **Health Ministers could be tasked in collaboration with appropriate colleagues with developing a set of principles to govern the use of genetic information in the insurance and employment fields. These principles might then be used to either inform appropriate provincial activities or form the basis of legislation or alternate action if such a measure is deemed to be required.**

12. **Health Ministers might also be tasked with determining appropriate mechanisms to ensure the involvement of people with disabilities in discussing the establishment of future parameters for genetic testing in healthcare.**

PATENT REFORMS

13. Working with governments, industry, researchers, patient groups and other stakeholders, the federal government should review the *Patent Act* as it pertains to gene patents. It is important to stress, that with appropriate balance a framework can be created that honours Canada's international agreements, protects healthcare institutions and providers while preserving the spur to innovation that the patent system is seen as offering in genetic research. The goal of the review should be modernization of the Act to achieve the objective of a fair and transparent patent review and approval process. This process should recognize the role of gene patents in supporting industry, but put in place appropriate safeguards and protections for healthcare, medical practitioners and researchers. Possible goals to direct the review would include:

a) Ensuring that appropriate protections are put in place to protect healthcare professionals and institutions, when using genetic materials in research or the provision of care, from legal action or the threat of legal action pertaining to patented genes or DNA sequences. This approach would therefore allow the continued use of different forms of testing (and their patenting) and different interventions each using some or all of the same gene or DNA sequence, but would not allow one gene patent to, in effect, control future subsequent medical use of that gene sequence or portion thereof.

b) Developing new patent office guidelines, procedures and training materials with regards to genetic patents, clear guidelines must be spelled out providing direction regarding novelty, non-obviousness and utility as they pertain to the issuing of genetic patents. Particular attention must be paid in this regard to Single Nucleotide Polymorphisms (SNP) and Expressed Sequence Tags (EST) patenting and include a determination as to whether and under what conditions these sub-gene patents might be granted.

c) Clearly defining the patentable subject matter to exclude broad-based genetic patents covering multiple potential uses and limit patents to clear and well-defined specific uses.

d) Clarifying the "experimental use" and "clinical non-commercial use" exceptions in the *Patent Act* to clearly indicate that non-commercial clinical use of patented genetic material and general research use of patented material are excluded.

e) Expanding the "methods of medical treatment" exclusion in the *Patent Act* to put in place explicit liability protections for medical practitioners and institutions for providing publicly funded medical services in the field of genetics including diagnostic genetic services using patented materials.

f) In light of recent developments in human cloning and moves in other jurisdictions to patent stem cell processes pertaining to the production of human organs, we would urge the federal government to consider adopting a public ordre morality clause within the Canadian *Patent Act*. Such a mechanism appropriately modified from the European experience would grant the Commissioner of Patents the ability to reject patents on processes, products and techniques which are deemed to violate Canadian morals and ethics. Such a power does not currently exist.

g) **Introducing an opposition period of nine months upon issuance of a new gene patent, based on the current European Patent Office model, to allow interested and affected parties to bring forward reasons for which the content, scope or validity of the patent should be reviewed.**

h) **Revising the compulsory licensing provisions in the *Patent Act* to cover genetic diagnostic and screening tests in the public healthcare system, thereby allowing the Commissioner the power to grant a compulsory license and to set an appropriate royalty rate after engaging appropriate industry and health sector expertise, if required, but without prior negotiation with the patentee.**

i) **Examining the creation of a specialized court to handle appeals of the Commissioner's decisions and to adjudicate in matters of patent validity and infringement.**

INTERJURISDICTIONAL CO-ORDINATING BODY

14. **Task Health Ministers with developing a draft terms of reference for a possible genetics Commission, setting out reporting relationships, core goals and objectives and role and responsibility vis-à-vis provincial resources and committees. The Ministers might also be tasked with determining appropriate funding sources for such an initiative, including federal resourcing as an option. This information could be brought forward to Premiers at a later date for decision.**

15. **Task Health Ministers with undertaking the groundwork required to promote a coordinated cross-jurisdictional approach to genetic testing. This task could begin with a detailed review of the types and forms of testing that are currently being undertaken by different jurisdictions and the setting out of some key principles and objectives that might form a future framework.**

SUPPORT FOR BIOTECHNOLOGY SECTOR

16. **Task Industry Ministers to explore priority areas to strengthen the biotechnology sector through a number of innovative means such as:**

    - **Examining the support to companies in the area of life sciences to encourage research, development and innovation. Such support could include increased funding for research and development, tax and investment incentives.**
    - **Continuing the practice of providing special federal funding for the regulation of biotechnology after 2002-2003 to provide resources for the anticipated 500 fold increase in biotechnology applications over the next decade.**
    - **Adapting the delivery of intellectual property services provided by the Canadian Intellectual Property Office (CIPO) to provide a sound, predictable intellectual property environment.**
    - **Involving the biotechnology industry representatives in discussions to ensure that CIPO provides globally competitve services for biotechnology patenting.**

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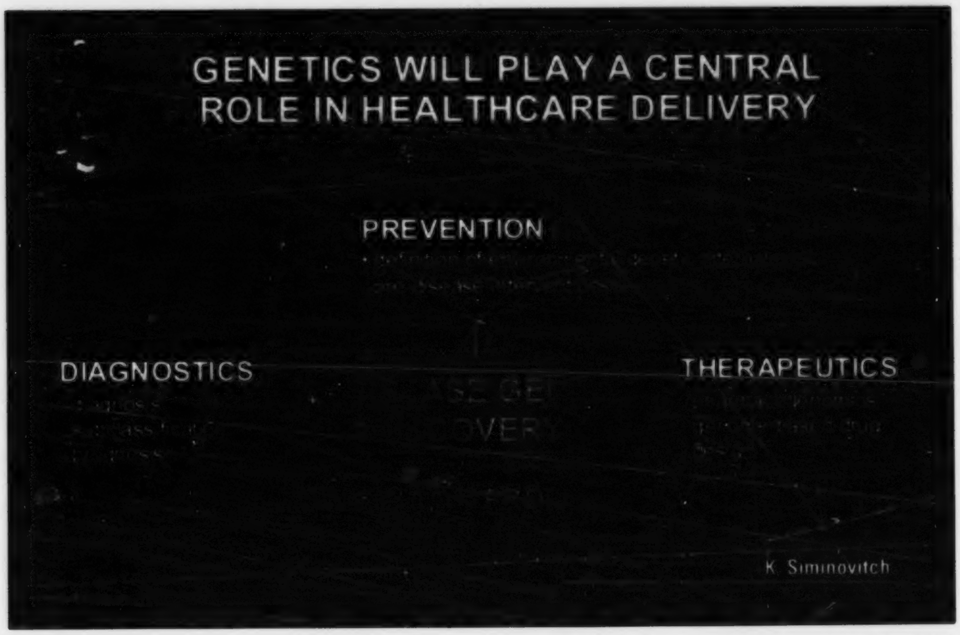
New Frontiers in Medicine

The multitude of recent and anticipated research developments in the fields of genetic information and genetic technologies hold out the potential to fundamentally redefine medicine within the lifetime of many Canadians.

The recent breakthroughs in genetics will, as many have noted, lead to major transformations in numerous aspects of healthcare, from diagnostics and disease management protocols, through to the variety of treatment options available to Canadians. These transformations will come regardless of whether the Canadian health system and Canadian society are prepared for them or not. Change will not come over night, it will be gradual and it will come in multiple forms, not all of which we can possibly know in advance, not all of which Canadian society can yet prepare for.

However, what we do know, even with the limited knowledge of the human genome that now exists, is that we face in the very near future, the introduction of new and potentially groundbreaking methods for managing, treating and/or identifying diseases and predisposition to diseases and conditions at a genetic level. Some of these advances have already emerged.

Researchers, healthcare professionals and society are learning more and more about the building block of human life (genes) and the possible applications of new genetic technologies. Increasingly genetic information is beginning to influence our understanding of both human health and the possibilities for healthcare. Information on human genes and the resulting technologies are moving healthcare forward into new terrain. An important part of this terrain will be increasingly shaped by public interest, demands and expectations. Demands and expectations not only for access to new tests, drugs and treatments, but ultimately an expectation of more from medicine.



GENETICS WILL PLAY A CENTRAL ROLE IN HEALTHCARE DELIVERY

PREVENTION

DIAGNOSTICS

THERAPEUTICS

K Siminovitch

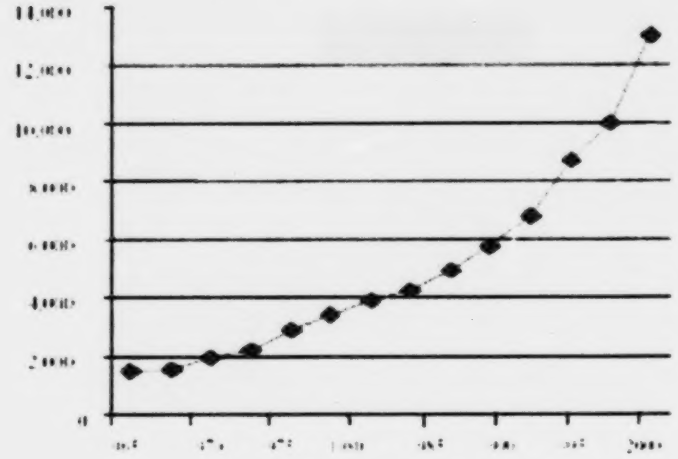
David Naylor, presentation, December 12, 2001[1]

A large part of this demand and interest no doubt will continue to be influenced by the ongoing media announcements of new breakthroughs in research surrounding genetics and genetic technologies. This interest is not unwarranted. Despite the hype that often surrounds new research breakthroughs and the considerable time and effort that often exist between a research breakthrough and a medical or diagnostic use, the reality is that there are sustained and ongoing research efforts in genetics. This research is resulting in new interventions, diagnostics and treatments which are beginning to be introduced into the direct delivery of care in Canada and more of them are on the horizon.

As with any major transformation, the hope offered by new techniques, diagnostics and treatments brings profound challenges. In some cases these challenges are unique to the field of genetics, in other cases the challenges simply highlight pre-existing weaknesses or policy questions in other areas which have not been addressed.

So, while it is probably true to say that the impact of the genetic revolution in healthcare won't be felt with full force for some time yet, beginning to develop the effective tools, policies and legislation to prepare Canada and our healthcare system for the coming changes needs to begin now.

NUMBER OF GENE - DISEASE RELATIONSHIPS



Ann Summers, presentation, December 2001[3]

It needs to begin now, because the impact of genetic technology on our healthcare system will inevitably be profound as new discoveries and tools for the treatment and/or prevention and diagnosis of diseases occur. **In Canada, it is estimated that 60 percent of Canadians will experience a disease with some form of genetic component during their lifetime.**[2] Genetic research and technology therefore, hold out the potential to help a large majority of Canadian people. If we look closely at the escalating utilization of existing tests, and public perception of genetics, it is clear that Canadians want, and indeed will demand in large numbers, access to these new technologies.

However, making genetic research tools or technologies more available as part of mainstream medicine will inevitably raise a multitude of issues. These issues will be broad ranging and include financial, ethical, legal, social and operational questions that will touch on all parts of Canada's publicly funded healthcare system. In their substance, though, many of the issues that will arise will go beyond practical challenges for the Canadian healthcare system. Many of the questions will touch on some of our core values and ethical beliefs, they will highlight tensions and force us as a society to define the boundaries of the acceptable and the unacceptable, the ethical and the unethical.

What should or should not be patented and how should those boundaries be defined? Should genetic tests for conditions for which no treatment exists be funded by the public system? What protections should individuals expect for their own genetic profiles? What do employers have the right to know and not know about their employees? How do we balance a fear of eugenics with the promise of genetics?

These are fundamental questions, questions which go beyond the strict boundaries of healthcare, but they are ones that Canada must, however belatedly, begin to face and resolve, if we are to jointly lay a solid basis upon which medical progress in the field of genetics can be responsibly embraced.

Clear policy, regulation and processes will be required to govern the future use of genetics in healthcare and to ensure that the system will be successfully equipped to benefit from the promise of genetic medicine. This transformation must take place even as medicine is already assimilating "new" genetic information into practice.

If we are to maximise the good that can come from the Human Genome Project, (HGP) (See section 1.3) provinces and territories have a responsibility, as indeed does the federal government, to put in place the forward thinking strategies and appropriate safeguards which begin now to establish the socially acceptable boundaries for genetics in healthcare. This means that all jurisdictions must come together to shape the course.

In shaping the course, profound questions will need to be asked and new solutions brought forward. Some of these solutions, such as recrafting the patent system to reflect the new realities of gene research, may be controversial and may take time to achieve.

However, jurisdictions must never lose sight of the fact that law is not an abstract concept. Law exists to codify values, to set boundaries and ultimately to reflect acceptable parameters for society. If the knowledge of the human genome forces us to rethink these boundaries, then rethink we should.

Other changes, such as promoting more co-ordinated access to both the review and provision of genetic testing across jurisdictions could potentially be achieved in a shorter time frame and build on the progress that has already been achieved in the realm of greater co-ordination with regard to pharmaceuticals.

Within Canada, a number of jurisdictions have already started to map out a rough path of how best to organise genetic testing into their health system. There is no doubt that there is much that individual provinces and territories can and need to do in their own jurisdictions. Much more, however, could be achieved through coherent and planned cross-jurisdictional co-ordination and collaboration.

This lesson has already been learned by a number of jurisdictions which have moved faster and with more forethought than Canada has to date. The United Kingdom has had in place a Human Genetics Commission (HGC) for several years now, grappling with and in many cases beginning to resolve, questions that have yet to even be asked on the Canadian stage.

Newspaper headlines such as, " Gene Tests Allow Disease-Free Baby[4] ", "A New Genetic Window on Curing Diseases"[5], "Researchers Discover Gene That Plays Role in Autism: Finding May Help Unravel Disorder"[6], are among the many found in newspapers on a regular basis.

An overwhelming majority of the media's portrayal of genetics tend to conclude with a prediction that this or that latest genetic finding will immediately result in new methods of prevention, detection, treatment or cure of certain diseases or disorders. In reality, years of research and development tend to be required to go beyond the identification of a specific mutation through to the development of an intervention or diagnostic.

Australia has launched a major commission on the role of genetics in society; governments across Europe have been engaged for a number of years debating the ethical boundaries for research, for commercialization, and for medicine.

The time has come for Canada to build on the enormous contributions that Canadian researchers have made to the Human Genome Project. We must work to establish the social, legal and procedural frameworks that will engage Canadians and ensure that the Canadian healthcare system and Canadian society are prepared to actively shape the future of genetics. To miss this opportunity will be to find ourselves continually reacting to scientific breakthroughs independently, in isolation, and with no coherent vision. Ultimately this can only be to the detriment of Canadian healthcare and Canadian society.

This report therefore seeks to provide provinces, territories and ultimately the federal government with a general basis for dialogue, as well as rough markers that we might choose to use to steer Canadian healthcare systems and support Canadian societies. These rough markers are no more than an attempt to aide us jointly in coming to terms with, and effectively managing, the challenges that come with the human genome era.

1.1 USE OF GENETICS IN MEDICINE

Basic genetics has long played a role in healthcare. The initial mapping of the human genome has, however, helped move the terrain toward the development of a greater number of practical applications of new and more specific knowledge.

Genetic research and technologies are being hailed for their positive contributions to healthcare. Certain genetic tests can now be used to diagnose diseases earlier than ever before. Individuals can opt to have a genetic test in order to find out if they are a carrier of, or if they have, a certain disease or predisposition to a disease. In some instances, this knowledge can open the door to lifestyle changes that can significantly alter the possible course of the disease, and/or reduce its onset thereby improving health. In addition, this technology is advancing treatment and/or other health interventions. For instance, health changes for certain conditions can now be better detected at the onset or early stages of disease, with the promise of better prognostic outcomes.

Amidst the excitement, it is important for healthcare planners not to lose sight of the relative role of genetics. A certain risk of progress in genetics, and one which we must strive to avoid, is the propensity for society to attribute an almost mystical power to genetics, when, in actual fact, more everyday determinants of health such as housing, nutrition, and employment have and will continue to play a dominant role in shaping the health of Canadians.

Much of the general interest in the role of genetics in healthcare is not unwarranted. In the field of pharmaceuticals, we can, for example, predict the development of new genetic approaches which increasingly allow for tailor-made treatments that are specific to disease-subtypes and individuals. Genetic research continues to help shape the development of assessment tools which will allow more and more treatments that are designed to be genetically compatible with the person that needs them. In doing so, new drugs will become available, likely with significantly reduced risk of adverse drug reaction.

These and other developments in genetic medicine, if appropriately harnessed, hold out some promise of more informed, cost-effective disease management practices and the identification of more relevant drug targets, which in turn will bring more specific drug therapies. [7]

However, these transformations will not be without initial and medium term costs. Beyond the additional incremental costs of new tests and treatments will lie other costs, those of ensuring that the Canadian healthcare system has access to the genetic expertise that will be required to effectively integrate genetic medicine into day-to-day practice. Outside of specialists in genetics per se, we will also be faced with a growing demand for genetic counsellors and we can assume that increasingly primary care providers (physicians, nurses and others) will need to have available the up-to-date training and skills in genetics that to date too few currently possess. The costs for such a process of transformation will not be easily borne by the system without a recognition of the need for funding not only to sustain the system, but also to allow it to evolve to provide Canadians with the benefits of the most advanced scientific breakthroughs.

Genetic related technologies are used for more than gene discovery. A host of supportive activities and economic niches have been generated by the biotechnology sector, activities that will begin to be increasingly felt in healthcare. These will include bioinformatics for genetic information storage and retrieval, and proteomics to characterize the total protein complement of a genome, to name a few.

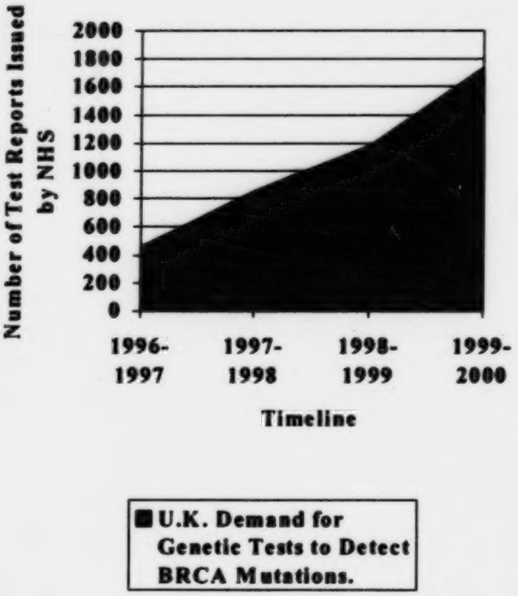
Outlined below are four key areas where genetic research is anticipated to have increasing practical and ethical impact on healthcare practices.

1.1.1 GENETIC TESTING

Genetic testing is an increasingly effective method used predominantly to diagnose a disease, to confirm a diagnosis of a disease or to detect the presence of a gene or genetic mutation which may indicate an elevated likelihood that a person risks developing a disease.

The testing of an individual by routine conventional diagnostic tests is often, but by no means exclusively, triggered by a patient displaying certain symptoms and responses. What tends to make certain forms of genetic tests somewhat distinct is that they are often used (with varying degrees of accuracy), to confirm the existence of a disease or predisposition to a disease in *asymptomatic individuals*. Technically, genetic tests involve the direct examination of DNA to look for particular gene mutations associated with specific diseases or with an elevated predisposition to a certain disease or condition.

Genetic tests are among the first commercial wave of medical applications stemming from new genetic discoveries and are being used more and more frequently by physicians. At present, there are at least 877 genetic tests available internationally to test for genetic disorders in children, adults and fetuses. Ontario geneticists already have in excess of 600 genetic tests available for use.[8]

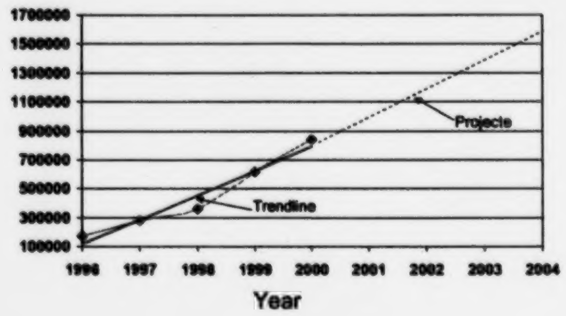


Genetic tests are currently being used to identify such conditions as: sickle cell disease, Down's Syndrome, Cystic Fibrosis, Hemochromatosis and breast and colon cancer. With the plethora of gene and single nucleotide polymorphisms (SNP) discoveries, the number of genetic tests being developed to detect diseases or genetic disorders is expected to rise well into the thousands over the next few years.[9] Increasingly, we can also anticipate seeing the form that genetic testing takes begin to change over time. Kit form testing will be made increasingly available, whereby a home testing kit can be ordered over the internet, a blood sample provided directly by the patient and sent to a laboratory, potentially outside Canada and the results of the test conveyed directly back to the individual.

Alongside the rise in the number of tests available will unquestionably be a rise in demand for the tests. We can see from the UK experience that once a genetic test is offered, the rate of uptake is often fairly dramatic (UK uptake for testing for the BRCA 1 and 2 gene rose by over 240% in the first four years of the test being generally offered).[10]

In Ontario, PSA testing for prostate cancer has increased 388% over a four year period from 1996 to 2000[11]. An increasing number of individuals are also requesting genetic tests from their physicians that they have heard of or read about through either the internet or mainstream media.

TRENDS IN COUNTS FOR PSA TESTING IN ONTARIO



THE EVOLUTION OF GENETIC TESTING[12]

Type of tests	Mainly diagnostic	Mainly predictive
Type of disorders	Rare disorders, mainly pediatric. Patients usually have a high chance of having, or developing, the disorder.	Common disorders with a genetic component, particularly adult-onset diseases. Patients may have low to high chance of developing the disorder.
Type of Results	Usually, but not always, confirm presence of disease but does not give information on its severity.	More complex risk predictions which may involve gene(s) and environment.

1.1.2 GENE THERAPY

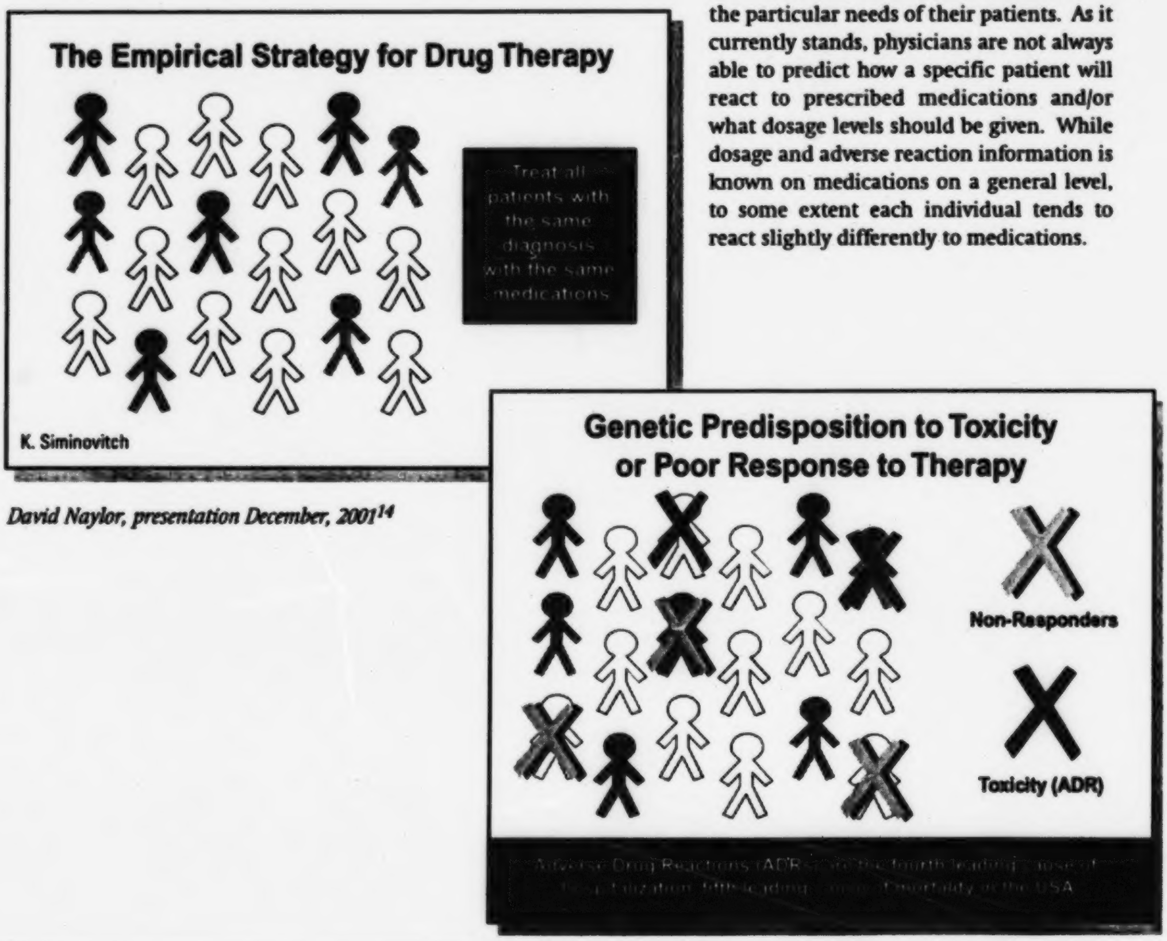
Gene therapy is a genetic development that targets specific genetic mutations (errors) in either somatic (non-reproductive) or germline (reproductive) cells. Gene therapy targets mutations in order to correct or delete them. Gene therapy differs from conventional medical treatment by addressing the underlying genetic cause of a disease at the DNA level rather than treating the symptoms. At its current level of development, it is thought that gene therapy is likely to have much success with diseases that are caused by monogenic or single gene defects, such as Cystic Fibrosis. This is because it can be simpler to identify single gene defects rather than diseases caused by multigenic factors (gene-gene interactions, enviroment, lifestyle etc.). To date, approximately 100 disease genes, that show primarily for monogenic disorders have been identified. Somatic cell gene therapy is currently underway successfully, but germline gene therapy is still being researched and developed in order to assess the implications, unintended or otherwise, for future generations. There have already been germline therapy trials with humans but after some questionable research practices, and considerable controversy germline gene therapy is currently being done predominantly and successfully with animals.

Gene therapy holds great promise to help further the understanding of the function of genes, clarify diagnoses and identify mutations. The greatest promise of gene therapy is that it may be used in the future (without a quality of life judgement) to prevent some diseases that are currently untreatable and cause great pain or suffering, or simply alter the likelihood that a person will develop a disease. One example of its progression can be exemplified by a study conducted at Harvard Medical School, where a new gene therapy technique has been used to cure Sickle Cell Anemia in mice.[13] This success has raised hopes of a similar development in humans, but the technique will need to be refined before human trials can begin.

Gene therapy is expected to target or eliminate mutated genes once it is deemed scientifically and ethically safe and effective to do so.

1.1.3 PHARMACOGENETICS/PHARMACOGENOMICS

Pharmacogenetics is the study of how genes affect the way people respond to drugs. By better understanding an individual's genetic response to certain drugs, physicians will be able to craft interventions that will fit the particular needs of their patients. As it currently stands, physicians are not always able to predict how a specific patient will react to prescribed medications and/or what dosage levels should be given. While dosage and adverse reaction information is known on medications on a general level, to some extent each individual tends to react slightly differently to medications.



The Empirical Strategy for Drug Therapy

Treat all patients with the same diagnosis with the same medications

K. Siminovitch

Genetic Predisposition to Toxicity or Poor Response to Therapy

Non-Responders

Toxicity (ADR)

Adverse Drug Reactions (ADRs) are the fourth leading cause of hospitalization, fifth leading cause of mortality in the USA

David Naylor, presentation December, 2001[14]

Beyond this, it is also unknown how effective or ineffective drugs might be for a particular patient and/or whether that patient will suffer from adverse effects. A stated long term goal of pharmacogenetics is to provide individualized medicine. Initial applications, are already being seen, in the area of drug discovery and clinical development. The genetic knowledge base is rapidly expanding to a point where physicians will soon be able to use DNA-based tests to aid in decision-making with respect to defining, with greater confidence, the most appropriate drug(s)and dosage to be given to each patient. An indication of just how valuable this type of testing might become is given by the example of TRUGENE HIV-1 test, recently made available in the U.S.[15] This genotyping test purports to offer physicians significantly enhanced information on an individual's responsiveness to certain medications and the particular resistance to medications that may be expected for that individual. Given the complex drug regimes that many people living with HIV currently face and the serious risk of drug resistance, this type of genotyping provides an example of why such enthusiasm exists with regard to some of the new approaches developing.

It is believed that a number of genes play a role in drug response. Further pharmacogenetic research is already underway to confirm and better identify the specific interconnections between genes and drugs.

By studying the different effects of a drug on gene expression throughout the entire genome, pharmacogenetics could greatly reduce the toll of insufficient or adverse drug reactions. If the promise of pharmacogenomics can be even partially achieved, this will mark progress of a very significant nature.

Adverse drug reactions have major implications for human health and the healthcare system. For example, **in the US, more than 100,000 people die each year from adverse responses to medications that are beneficial to others, 2.2 million experience serious reactions, and unknown numbers of people fail to respond** at all. Adverse drug reactions are one of the leading causes for hospitalizations in the US (1.5 million cases per year, 100 000 deaths, 4th - 6th cause of mortality). [16] Although data on Canada is limited, **there is nothing to suggest that adverse events are less likely to occur in Canada than in the U.S** Extrapolating from U.S. statistics. It can be estimated that up to 10,000 deaths per year from adverse reactions to medications occur in Canada.[17]

The traditional approach to medical care will change radically as genetic knowledge allows treatment and prevention strategies to be tailored to individuals rather than having it based solely on good judgement and trial and error. Drugs that will target individual patients will be developed. This advent of individualized drug therapies will also carry with it immense challenges for how provinces and territories determine and administer drug coverage and eligibility criteria for general and restricted use medications.

For pharmacogenomics to more completely fulfill the promise of targeted interventions, clinical and epidemiologic studies are urgently needed to assess how drug response varies among individuals with different genotypes, what the prevalence of relevant genotypes is in the population and in relevant subpopulations, and whether and to what degree other environmental factors interact with genetic factors to influence drug response. Relative effectiveness and cost effectiveness to existing treatments also warrant fuller examination. Clinical trials and observational epidemiologic studies are crucial for providing us with the population-based data needed to use pharmacogenomics in the practice of medicine and public health.

REFRACTORINESS (NEGATIVE REACTION) AND/OR INADEQUATE THERAPEUTIC RESPONSIVENESS TO MAJOR DRUG CLASSES[18]

[illegible]	[illegible]
Beta-blockers (heart disease, high blood pressure)	15 – 35%
ACE inhibitors (high blood pressure)	14 – 37%
Angiotension 2 receptor inhibitors (high blood pressure)	12 – 29%
HMGCoA reductase inhibitors (cholesterol)	11 – 33%
SSRIs (depression)	9 – 35%
Tricyclics (depression)	20 – 57%
Steroid - 5_ reductase	30 – 80%
5HT1 (migraine)	20 – 45%
_-interferon (hepatitis C)	30 – 70%
Anti-neoplastics	20 – 80%

David Naylor, presentation December, 2001

Pharmacogenomic developments for drug safety and effectiveness are undeniably positive, but may not benefit everyone.

Where the category of consumers for a drug is relatively small, market forces could either dictate a higher price or less research and development for the drug. In pharmacological research, drugs that benefit fewer people in the population are sometimes called "orphan drugs" and legislation and incentives have been created in a number of jurisdictions to ensure that research and development is done for these drugs. In the genetic era, consumers may be defined not only by the condition for which treatment is being taken, but also by a particular genotype.

How will pharmacogenomics affect the criteria for deciding which drugs to develop and for whom? What forces, if any, will ensure that all segments of the population are included in the drug development strategies undertaken? These are questions that we cannot yet begin to answer.

While reducing the number of hospitalizations from adverse drug reactions is undoubtedly a goal that all would support and one which, in the longer term could potentially reduce pressure on hospital beds, we do not yet know at what cost this transformation will come . Between 1985 and today, Canada's drug expenditures have grown at a rate twice that of the overall rate of growth for the healthcare sector. Rising in the range over 10% annually in the last five years, costs for prescription drugs reached $12.3 billion in 2001.[19]

As new pharmacogenetic and pharmacogenomic interventions are initially introduced we can anticipate that the short term costs will be high and, while pressure may be relieved elsewhere in the healthcare system as a result of more successful interventions, reduced pressure in hospitals does not necessarily equate to more funding available to drugs. Given competing pressures for various health services the net savings in real terms to the health system will be difficult to capture, while the costs of the interventions themselves will be difficult to avoid.

In addition to the cost of drugs themselves will be the cost of genotype screening to determine receptivity to one or more families of medications. It is anticipated that the costs for genotype screening will not simply be for a test in isolation, there will undoubtedly be costs associated with the necessary counselling and advice provided by a physician working with a patient on a range of treatment options.

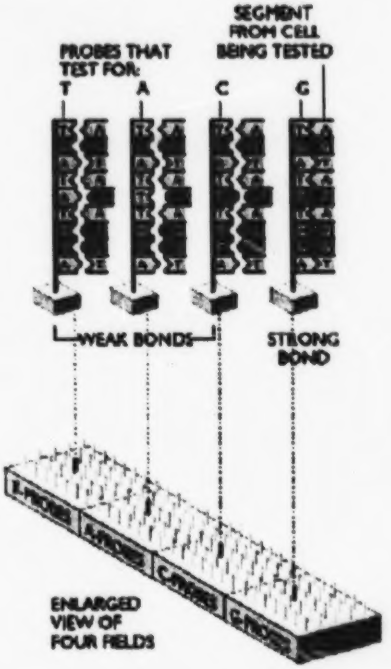
Work in pharmacogenetics/pharmacogenomics is yet another way in which genetic research and technologies will change the face of medicine through better and safer drugs, more accurate methods of determining appropriate drug dosages and improvements in drug discovery and development processes. While this work heralds great advances for Canada's publicly funded healthcare system, the challenge of effectively harnessing the long term possibilities of pharmacogenetics/pharmacogenomics will need to be met at the same time as we face the immediate and pressing challenge of simply maintaining existing pharmaceutical expenditures with very limited additional resources available.

1.1.4 THE DNA CHIP

The DNA chip (also known as the biochip or the gene chip) has been heralded as another potentially major technological contribution to the changing genetic frontiers of medicine. The DNA chip represents a fusion of research and technology development from the field of information technology with that of DNA sampling and genetic research.

The DNA chip uses microchip technology to dramatically accelerate genetic studies. DNA chips can gather genetic information at twenty-five times the rate of traditional methods. In fact, DNA chips helped dramatically to accelerate the work of the Human Genome Project. If DNA chip development lives up to its promises, it will enable clinicians or even patients themselves to quickly and inexpensively test for up to 20,000 to 30,000 genetic properties from a drop of blood or hair sample.[20]

Using the DNA chip, diagnosis of a genetic condition could be done in a few minutes and hundreds of tests could, in theory, be carried out simultaneously. It has been estimated that this genetic technology can be used to scan up to 400,000 samples within five minutes. DNA chips make routine or large-scale screening quite simple and also make it possible to monitor the effectiveness of patient therapies and investigate the complex interactions, dependencies and information that flows between genes.



This graphic shows how a DNA sample is screened by a DNA chip. The DNA sample is broken into small fragments and treated with fluorescent dye. The chip is then immersed in the sample DNA. The small fragments bind to complementary dry "snippets" on the DNA chip. A special machine then reads the chip and interprets which snippets on the chip were bound by the same DNA sample.

J.Isaacs [21]

DNA chips could greatly facilitate genetic research as medicine now becomes able to work from the bottom up (from gene to receptor protein to potential drug).[22] There are also a number of clinical applications for this technology. For example, DNA chips could make it possible to identify the precise strain of bacteria that is causing an illness, and the exact antibiotic that is needed can be developed from the information.

In combination with pharmacogenetics, DNA chips could reduce the number of adverse drug reactions and increase the efficacy of antibiotic prescriptions.[23] Also, in a very recent study scientists have used gene chip technology to distinguish between acute childhood leukemia and other types of leukemia that is not acute or is of "mixed lineage". With this discovery, gene chip technology has in effect defined a new disease using whole genome expression profiling to do so. This discovery has been heralded as bringing a new era of molecular diagnosis.[24]

DNA chips are in existence now and companies are preparing to bring their products to market. However, major technological and regulatory challenges need to be addressed. Companies are also undertaking further research and development to find ways to increase the number of tests that can be done on a single chip, increase the rate of chip production to meet expected demands, and lower costs. Currently, DNA chips cost between $100 to $450 (USD), however, according to DNA chip producer Affymetrix, DNA chips that instantly detect the activity of tens of thousands of human genes could shortly be available for as little as $5 (USD).

The potential that DNA chips offer in terms of being able to do a large number of tests in a very short time is enormous. The technology opens up the possibility of being able to perform many tests at one time and may as a result reduce the cost of tests. However, with the vast array of information DNA chips produce, many questions surrounding the consequence of their use will arise. These consequences lead one to question whether just because a technology exists, should it be used?

When patients now undergo genetic tests, it is routine in many jurisdictions offering genetic testing for both pre and post-test counselling to be offered. This is done to inform the individual of what a test can and cannot reveal, discuss the availability (or lack of availability) of treatment options, and to assist an individual in understanding the meaning of his/her test results.

DNA chips potentially open a whole new set of problems. Most genetic testing presently undertaken and the accompanying counselling is predicated on performing a limited number of specific tests for a limited number of specific conditions or predisposition to a specific condition, not upon multiple testing.

If multi-gene DNA chip testing is to be made available to the public, the question arises as to the manner in which technology gets deployed. If the technology is simply used to perform specific individual tests more rapidly, accurately and cheaply than is conventionally possible then only limited issues arise. If however, the technology is deployed in a manner which allows for (or actually undertakes) simultaneous testing for multiple genetic markers of different conditions, then the technology becomes more problematic. For instance, how can a clinician or counsellor possibly prepare an individual for the results from simultaneous testing for multiple conditions or predictive markers. In a matter of minutes a patient could potentially find out that they have genetic markers associated with a number of diseases or disorders.

While the presence of these markers might indicate an individual's enhanced predisposition to a particular disease, the important role of other factors (eg lifestyle, environment) and their interactions must also be considered and be a key part of the informed discussion of test results.

The sheer volume of information resulting from the use of DNA chips could prove to be overwhelming to both patients and healthcare professionals. In an era where physicians have greater time demands and where public perceptions of genetic risk are far greater than the evidence would always suggest, the implications of such testing will need to be fully explored if we are to avoid the potential harms that can come from ill-advised treatment decisions made on the basis of such testing. Very careful attention will need to be paid in determining whether patients will be offered the multiple tests that might theoretically be possible using this form of technology or only such condition-specific tests that their healthcare providers deem necessary.

Other issues will undoubtedly emerge. Some while not unique to the DNA chip such as the use, storage and access to test results, are brought into very stark relief by the sheer volume of information generated by the use of this technology. The DNA chip certainly cannot be held responsible for the overall issue of genetic privacy. It will, however, bring the issue into the forefront as the chips move into application.

1.2 GENE PRIMER

In order to make sense of the breakthroughs in genetics, some basic concepts and definitions are needed surrounding genes, genetics and genetic technologies. The following presents a bare bones description of genes and gene mutations.

1.2.1 GENES

Genes are often referred to as "the building blocks of human life". This reference stems from the fact that they instruct all living organisms on how to develop. In essence, they develop a "blueprint for life". Genes are responsible for determining many human traits such as eye colour, blood type and even an individual's predisposition to certain diseases.

Human offspring inherit genes from both biological parents. Physically, genes are units within cells made up of deoxyribonucleic acid (DNA). Within cells, genes are organized into chromosomes, of which humans inherit a set of 23 chromosomes from each parent. In interaction with the environment, chromosomes determine physical and possibly even some human behavioural characteristics. The structure of genes, DNA, is made up of four nitrogen bases (A, T, C and G) that can be combined to make up to 64 different sequences. In many respects, DNA can be thought of as a code word, consisting of four letters (A, T, C and G). Each code word instructs the human body to produce proteins. Proteins then provide instructions to the body. In order for the genes to continue to provide instructions to proteins, DNA must be replicated.

DNA replication is a process whereby DNA makes an exact copy of itself. By doing so, DNA ensures that the proteins continue to receive and carry out their instructions. Cells in different parts of the body replicate according to different schedules and once they receive information from the gene or replicated gene, they instruct the body on what to do. To exemplify with human hair, DNA replication directs the proteins to work continuously, in other words to grow hair, and DNA replication ensures that proteins direct the body to grow hair everyday. However, sometimes errors occur during DNA replication that can be the cause of gene mutations.

1.2.2 GENE MUTATIONS AND DISEASE

When there is a problem in the replication of genes, mutations can occur. Genes with mutations can also be inherited from biological parents. Gene mutations can result in disease by altering a gene's function or affecting the production of proteins.

All human inherited genes have either dominant or recessive traits. In terms of inheriting mutated genes, the genes can be either dominant, recessive or sex linked. These three types of gene inheritance are described below.

A dominant trait

A dominant gene affects the person who inherits it. This means that in order for the gene (and the trait it brings) to be present, the person only has to inherit one copy of the relevant gene. In other words, if the gene is passed on from either parent, the offspring will have the trait the gene brings. To exemplify, a disease caused by an inherited dominant trait is Huntington's Disease. If one parent has the gene for Huntington's Disease and passes on the gene to their offspring, their offspring will develop the disease.

A recessive trait

Unlike dominant traits that can be inherited from one parent, recessive traits must be inherited from both parents. This means that both parents have to have the gene and both parents would have to pass the gene on to their offspring in order for the trait to be present. If a person inherits a recessive gene from only one parent that person will not develop the trait but will be a carrier of the recessive gene (meaning that they can pass the gene on to their offspring). Cystic Fibrosis is an example of a genetic disease caused by the inheritance of a recessive trait/gene from both parents. In the case of Cystic Fibrosis, both parents would have to pass the gene to their offspring in order for them to have the genetic disease.

Sex linked traits

An abnormal gene on the X chromosome from each parent is required to cause a sex linked disease in females since females have two X chromosomes. Males however have only one X chromosome. Therefore, a single recessive gene on the X chromosome will cause the genetic disease. Recessive genes on the X chromosome of the male will be expressed. In humans, at least 320 diseases are thought to be X linked, they include hemophilia, congenital night blindness, high blood pressure, and Duchene Muscular Dystrophy. There is also thought to be at least a dozen Y linked genes in addition to those that code for masculine physical traits.

1.3 THE HUMAN GENOME PROJECT (HGP)

The HGP is an international research program that was designed to construct detailed genetic and physical maps of the human genome (the complete set of human genetic material). HGP's goal was not only to speed up the process of mapping the entire human genome, but also to ensure that the information it maps is put into the public domain for use and development by scientific, medical and other researchers and healthcare professionals. HGP's ideology for making its information publicly available is to afford the opportunity for the public to expand on, further develop and create genetic discoveries and tools from it. Sixteen countries are a part of this international effort and Canada is one of them (see box on page 18 for more information on the Canadian contribution to this effort).[25] The result of rapid advancements and promises is an explosion of innovation and entrepreneurship that will enrich the economies of participating nations while possibly enhancing the quality of life of humanity. There is naturally a rush by participants to discover new genes and to seek protection of intellectual property through patents.

The HGP is perhaps the single most ambitious project of its kind and has forever revolutionized the world of gene research. Not only has it vastly expanded the understanding of human genes, it has thrust the issue of gene patenting into the forefront of research, medicine and society. To date, HGP has led to the identification and mapping of 30,000 genetic sequences, containing approximately three billion base pairs of DNA. A draft of the human genome was published in February 2001. All of the public information from it promises to revolutionize the processes of finding chromosomal locations for disease-associated genes. Already, the draft of the human genome is enabling researchers to find genes associated with a number of genetic based diseases and disorders. So far, over 30 genes have been pinpointed and linked with diseases such as breast, skin and colon cancer, muscle disease and Alzheimer's disease. The draft sequence has also created a paradigm shift in that it has created an entirely new approach to biological research. In the past, researchers studied one or a few genes at a time. Now, whole genome sequences can be studied at once and new methods for diagnosis, treatment, and/or prevention are approached on a large scale. Researchers concurrently see how tens of thousands of genes and proteins work together in interconnected networks; while on the other hand, they can pinpoint genes or narrow their studies to all the transcripts in a particular tissue, organ or tumor.

Scientists working on the project have also identified approximately 1.4 million locations where single-base DNA differences (single nucleotide polymorphisms or SNPs) occur in humans. Along with the first draft of the human genome, the HGP in cooperation with the private sector has produced SNP maps that have identified DNA sequences underlying such common diseases as cardiovascular disease, diabetes, arthritis, and some types of cancer. By identifying disease genes and SNPs, researchers are able to target the development of effective new therapies.

It is commonly believed that the full sequence of the human genome will ultimately lead to a vast array of new or specific targets for diagnosis and drug therapies. Already, preliminary new treatments are being envisaged based on newly found genes for asthma, Alzheimer's disease, and mood disorders such as depression. However, as one of the concluding sentence of the human genome sequencing paper states:

> **"It has not escaped our notice that the more we learn about the human genome, the more there is to explore"[26]**

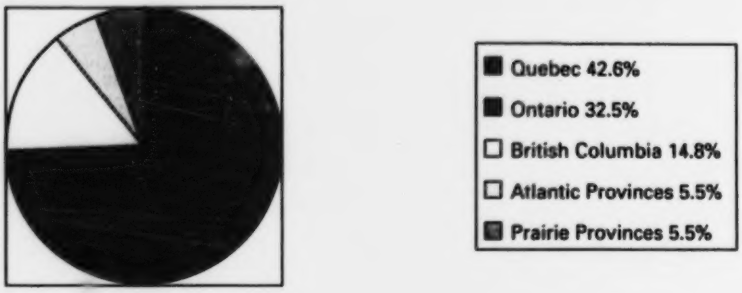
The first human genome draft sequence was hailed as the most significant contribution to the "new" genetics but the genetic revolution is just beginning. It is of utmost importance that the information from genetic research and discoveries are made publicly available in order to build on and use tools for the improvement of human health and well being. The success of the HGP has generated much hope and opportunity in the study of disease and disease therapy. Success in characterizing the genomes of other species and the isolation of novel genes has presented humanity with powerful tools to modify and genetically understand humans and other life forms.

1.4 CANADA'S ROLE

Canadians will benefit and have been actively contributing to the developments in genetic research and technologies in many ways. Canada's participation in the HGP was co-ordinated through Genome Canada, a non-profit corporation dedicated to developing and implementing national strategies in genomic research to benefit Canadians. A key national infrastructure component that supports collaboration among genome research centers is the Ontario Centre for Genomic Computation. This Centre, which is home to the international Genome Database, also ensures that Canada has a central role in global genomics initiatives.

Canadian researchers have been at the forefront of many gene and genetic technological developments. A significant Canadian advancement in gene therapy, for example, occurred in January 2000 when Toronto researchers announced they had succeeded in injecting a patient with a DNA treatment to encourage the growth of new blood vessels in the heart. This announcement signified the beginning of a major gene therapy clinical research program for heart patients. In addition to this, in November 2000, an international team involving Canadian researchers reported they had successfully cured Type 1 (juvenile-onset) diabetes in rodents. The researchers hope that this breakthrough will lay the groundwork for the development of gene therapy that will cure Type 1 diabetes in humans and go on to further genetic research.

GEOGRAPHIC DISTRIBUTION OF CANADA'S GENOMIC COMPANIES



The Canadian genomics industry is a strong and rapidly growing component of the world's second largest biotechnology industry. According to Genome Canada's Genomic Companies directory,[27] there are at least 54 companies in Canada capitalizing on innovative Canadian research in the areas of genomics and proteomics. Of the 54 companies, 40 have declared gene discovery as an activity. Financially, at the end of 2000, the Canadian genomic industry had nine publicly traded companies with a total market value of $1.5 billion. The leader of these nine companies was Ontario's Visible Genetics Inc. (OVG). OVG had a market capitalization value of $826.2 million and GLYCODesign Inc. with $136.8 million. Other significant companies are Ecopia Biosciences Inc. and Signalgene Inc. in Quebec at $226.0 million and $97.5 million respectively. The geographic distribution of Canada's genomics companies as illustrated above breaks down by region with Quebec 42.6%, Ontario 32.5%, British Columbia 14.8%, Prairie and Atlantic provinces each 5.5 %.

To continue excellent achievements, Genome Canada received $300 million from the federal government in February 2000 to establish five research centres across the country: Genome Atlantic, Genome Québec, Ontario Genomics Institute, Genome Prairie and Genome British Columbia, administered through Genome Canada. Approximately 10 per cent of this funding will support Genome Canada and 90 per cent will support the research and development activities of the five regional genomics centres. In addition, the federal government recently announced (November, 2001) an additional $136 million awarded to the five genomic centres.

In March 2001, Genome Canada committed to funding 22 projects across these centers. The various projects have an emphasis on healthcare and some topics include the science and technology of genomics and proteomics, their ethical, legal and social issues and the relationship between the environment and genomics and proteomics. In addition to this, Canadian governments have been quick to realize the importance of supporting research and development of genomics at the university level.

SOME CANADIAN CONTRIBUTIONS TO GENETIC RESEARCH

Canadian researchers have made key contributions to genomics.

- The gene responsible for Duchenne and Oculopharyngeal Muscular Dystrophy were identified.
- The gene defect that causes one form of Tay-Sachs disease was identified.
- Researchers discovered the gene responsible for Cystic Fibrosis.
- Researchers identified the gene responsible for Wilson disease – an inherited disorder in which copper accumulates in the liver and is released to other parts of the body, leading to severe liver and brain damage.
- Researchers discovered two genes responsible for early onset Alzheimer's disease, the most severe form of the disease.
- Researchers discovered a gene responsible for colon cancer.
- Researchers discovered a chromosome 13-linked breast cancer susceptibility gene.
- Researchers identified a gene called CRX, which causes cone-rod dystrophy, a condition which leads to the degeneration of the retina's light-sensing cells, the photoreceptors.
- Researchers discovered the gene which causes Lafora disease, a severe form of epilepsy.
- Researchers discovered a gene responsible for sacral agenesis, a defect in spinal development.
- Researchers discovered a gene that is frequently overexpressed and contributes to the progression of breast cancers.
- Researchers identified a region on chromosome 19 that contains a gene that modifies the severity of Cystic Fibrosis (CF).
- Scientists identified a gene that causes a metabolic disorder affecting the liver.
- The gene responsible for a form of kidney disease, and a corresponding diagnostic test are identified.
- Researchers linked activity of cancer-causing genes to normal wound healing process using a fruit fly model.
- Inherited prostate cancer gene identified.
- Dr. Michael Smith won a Nobel Peace Prize in Chemistry for providing the world with one of the key tools for genomics research.
- Canada ranks second in the world in terms of patenting activities to the U.S. and is sixth in the publications of scientific papers.
- The Human Genome Database (the repository for all knowledge concerning the role of human genes) is housed at The Hospital for Sick Children (Toronto). The hosting of and joint development of the database is another of Canada's vital contributions to the greatest medical revolution of the century.

1.5 WHERE WE ARE NOW?

Although significant strides have been made in unraveling the human genetic code, discovering genes and developing genetic technology, the work is far from complete and the results will remain unknown without a great deal of further research.

As more gene functions are discovered more information about humankind will be discovered. With the growth of genetic information, scientists continue to revise and recalculate the number of genes in the human body. Before the first draft of the human genome in 2001, scientists estimated that humans may have approximately 100,000 genes, this was subsequently revised to 30,000 to 40,000 with the initial description of the human genome. More recently however it has been calculated, and some new studies have concluded, that humans may have between 65,000 and 75,000 genes.[28] Nonetheless, even at this preliminary stage of discovery, extraordinary medical advancements have been made; various sources state that, anywhere between 600-4,000 diseases or conditions are gene related.[29]

As the findings of genetic research are further integrated into medical practice, the understanding of human illness and condition will increase exponentially. There is little doubt that gene-based medicine is going to fundamentally change the delivery of healthcare.

The growth in genetic-based medicine will necessitate many changes in healthcare delivery both at the individual and system level. Further understanding of genetics will prompt the development of new or modified diagnostic and treatment models. Such services may include population-based or individual screening for specific disorders, presymptomatic medical therapies and ways to meet the challenges of greater precision in diagnostic techniques. Understanding the psychological effects of this knowledge on individual health and appropriate counselling will also become an increasingly important component of medical care and treatment.

The Canadian healthcare system will also need to develop new ways of classifying disease, facilitating the discovery of new and better medicines, and personalising medicine, by enabling doctors to prescribe medicines to patients who are likely to respond and not suffer serious side effects. The Canadian healthcare system needs to offer the possibility of earlier detection of disease, and enable doctors to focus on prevention as well as the treatment of disease, through models developed from genetic discoveries.

1.5.1 WHERE WE ARE NOW WITH GENETIC TESTING[30]

Prenatal Diagnosis: Over the next few years, we will likely see a declining use of cytogenic analyses for screening abnormalities as maternal serum screening and ultrasound testing become more refined. Cytogenics will be used to confirm a screening result. Fewer tests will be done, but a higher proportion of those tests will be abnormals and will require greater test sophistication. At the same time, there will be an increase in molecular and biochemical testing and test methodologies will expand and become more accurate.

Pediatric/Developmental Testing: Cytogenetics will continue to be used and, with other technologies, will provide rapidly increasing diagnostic standards. Cytogenetics will continue to be used until chip technology is practical. More tests will be developed for more diseases, and the results will likely be more accurate. These trends may result in higher costs and greater overlap among test methodologies.

Adult Genetics: The focus will be on unravelling the complex interactions involved in diseases that involve interaction between genes, lifestyle and the environment. This will mean increased use of gene-based testing to identify those at increased risk for common adult onset diseases.

Cancer Genetics: The indications for diagnostic genetic testing will continue to expand, and will cover a wider range of tumours, reoccurring disease, gene-profiling for tumours and gene-based therapeutics. It is believed that there will be an increase in predictive testing for common cancers (e.g., breast, ovarian, colorectal, skin tumours), and in the overall demand for testing because of the increasing number of people living with cancer.

> **Our healthcare system ...(is still) in an era of half way technologies. We can palliate or mitigate many diseases, but cannot offer definitive cures or transformative and permanent improvements in health status. At the moment, all we can do is make life better and longer for a larger clientele. We must consider the impact of genetic medicine on further genetic research and technologies as well as health system utilisation."[31]**

There is "good" research and there is "undesirable" research. There will be good tests and bad tests. Some will be productive to the health system and the health of Canadians and some will be extraneous and create more "half way technologies" rather than completing those already in existence. It is important for Canada to develop the technologies to the point where they will be useful and advantageous, and not simply add to the growing financial albatross by creating demand without a source of supply and without proven utility.

Although we are just beginning to learn about genetic tools there is already a growing reliance on them. For example, the use of proteomic and bioinformatics to make sense of or explain health and illness. Genetic proteomics are becoming a way of life in determining treatment of certain diseases or disorders. Also, genetic testing is playing a greater role in diagnosis, prognosis, assessing remission/relapse status and quantifying residual disease.[32] While the contributions that genetic research is making vary according to disease, genetic medicine is drastically changing how disease is viewed and defined.

As genetic tools are being used more frequently by healthcare professionals debate is increasing as to where they should fit into the healthcare system. Not only this, but the public expects new products from genetic research. Canada will have to try to emphasize strategic investment into research that develops useful tools rather than "half way technologies". As the public demand for current genetic technology increases, it is important that the public is informed of the barriers that could prevent the use of genetics tools we have now in healthcare. Some barriers include costs of diagnostic equipment, issues concerning the reliability of tests and the lack of consensus on ethical issues surrounding their use.

2. Challenges to Existing Frameworks

As with any other technological innovation, the increasing knowledge of human genetics and the corresponding developments in testing and treatment will prompt a major paradigm shift in the organisation and delivery of certain aspects of healthcare. Existing frameworks will need to be modified. Some have even gone as far as to say that the impact will be as significant as those experienced when antibiotics and vaccines were first introduced.

The ability to predict and/or alter future health conditions, in advance of their manifestation also promises to reconceptualise traditional notions of health and disability and create new categories of disease. The dominant paradigm of "diagnose and treat" may, for some diseases and conditions, eventually be eclipsed by a framework of "detect and manage".

Incorporating genetic technologies into mainstream medicine is occurring little by little. With or without timely government action, Canada will end up re-examining some fundamental components of its healthcare system and indeed of our society.

Genetic testing and screening will present novel challenges, not the least of which will be funding and resource allocation. To what extent should certain predictive genetic tests be publicly funded or privately available and if so, how will we determine where the boundary of "medically necessary" is drawn and under what regulatory framework will these tests exist?

These are not easy questions to answer and the tension between the desire of individuals to access certain forms of predictive testing ("the right to know") and the actual health benefits that could accrue from having the test will be difficult to resolve.

The broader adaptation of genetic testing and the wider dissemination of genetic information will also bring calls for new legislative frameworks and policy initiatives to protect genetic privacy and prevent genetic discrimination.

Accepted practices with regard to informed consent and the protocols surrounding the testing of children will face questions and challenges that have not been experienced before.

Preparing our healthcare system for these challenges will be a long-term task. It will range from reassessing the training that is offered at medical schools and in continuing medical education, reassessing the balance of skill-sets required in the health system, through to changing the way care is organized and delivered. In health policy we will increasingly need to determine the best frameworks within which to make the difficult choices that genetics will pose in the years ahead.

2.1 NOT "JUST" A TEST

Many conventional medical tests are usually undertaken to detect evidence of a disease or a condition that is already present, or in the early stage of the pathological process. Predictive genetic tests, however, detect the genetic markers which can indicate an elevated potential for developing a disease well before the condition has developed or before symptoms have appeared. In many circumstances the actual risk of a disease or condition developing will be based upon multiple factors, only one of which may be genetic.

We are only just beginning to work through the ethical, social, and psychological implications of this type of knowledge for individuals, families and society. As testing moves into more and more areas, these implications will become far more apparent and demand greater and greater attention.

At the present time, most predictive genetic tests are only imprecise measures of risk. The science is still relatively new and much is still to be learned about the complex interplay between genes and the environment. A disjunct exists, however, between the state of science, the role of genetics, and the beliefs of the public that many genetic tests regardless of type are definitive proof of having a disease or condition.

It is for this reason that the early genetic testing that has been established in Canada has tended to be highly organized and structured around extensive pre and post test counselling.

Pre and post testing counselling by a qualified genetic counsellor is an essential component of genetic testing, as is follow-up counselling. The reasons for such an emphasis on information and counselling is precisely because the test is not simply a "test" and the results will often not be black or white but will require an individual to make a series of sometimes painful and complex lifestyle and treatment decisions.

For instance, the results of pre-symptomatic testing for mutations of genes associated with breast cancer may influence a woman to undergo a preventative mastectomy, a decision no woman makes lightly.

The ethical principle of avoiding harm is also raised around the question of whether predictive testing should actually be conducted when no effective prevention or intervention is available. This will not be an easy determination to make in some cases, where, even if a test could reveal a very high likelihood of an incurable disease, one can anticipate that there will be arguments brought forward that the individual or the individual's family has a right to know. Likewise the individual could make major changes to his/her lifestyle, if only the knowledge was available. Saying no in certain complex cases may be extremely difficult to do.

How realistic is this scenario? In a recent survey 67% of respondents said that they would very likely or somewhat likely take a genetic test that was recommended by their doctor even if the disease or condition to be tested for did not have a cure.[33]

Furthermore, even when there is a cure, the determinations are not easy. Treatment options will differ widely depending on the nature of the genetic condition indicated by the test. It is important for our health system to understand the health economic consequences of particular genetic tests beyond the simple questions of the sensitivity, specificity and cost of an individual test.

For example, where the prevention of a certain condition (which may have only a small genetic component) requires only simple and inexpensive lifestyle changes to significantly reduce risk, or where there are no current methods of treatment or prevention, the value of testing decreases to the point that publicly-funded systems must ask "what is the added value?"

Genetic testing regimes must therefore take into account not only predictive accuracy and implement procedures to further minimise harm but we must always consider the tests within the broader objectives of the health system as a whole. This focus will not be easy to maintain as a broad range of predictive tests become available commercially south of the border and at a distance via internet sites.

Ultimately then, genetic testing is always about more than a test itself, testing is simply one part of an organized regime of care and is ideally just one component of a genetics program which itself is simply one part of our health system.

The requirements of formalized genetics programs however impose heavy staffing, facility and funding requirements on an already burdened healthcare system. With an expansion of demand for testing and a broader range of tests becoming available, the resource demands of genetics programs relative to other components of the healthcare system will undoubtedly grow significantly.

Facing the financial constraints that it does, the publicly funded health system is likely going to be unable and/or unwilling to fund all of the predictive genetic tests that individuals may desire. The desire to "know", however, will undoubtedly exceed what most publicly funded healthcare will consider beneficial or medically necessary. In this case, we can anticipate a growth in private genetic services in some jurisdictions to fill the public demand. Quite possibly this will also take the form of kit-based tests and include direct marketing to the public.

We can anticipate that in the coming years that a significant regulatory and policy challenge could well arise from the expansion of private genetic testing services. The appropriate means to regulate and manage such an expansion will need significant thought and conventional models may need to be re-evaluated. We will also need to understand what the potential health human resource challenges will be for the publicly funded system if such a development should occur.

While the tests that may come to be offered privately may be deemed not to be medically necessary, the actions taken by individuals on the basis of information received are potentially very significant, both to the individuals' own well-being and health and also to the services and programs utilised in the publicly funded system. An improved capacity to track these impacts and monitor and respond to the implications will be required by all health system planners.

2.2 PRIVACY, DISABILITY AND DISCRIMINATION

All personal health information is sensitive, perhaps the most sensitive information about us as individuals. What is so special about genetic information?

We have all, at one time or another, had a family history taken by a physician. In some ways this is the closest thing in conventional health information to genetic information. There is one crucial difference, a family history can be partially missing, it can be inaccurate, it can be concealed or it can be withheld.

A genetic test result, while it may be inaccurate, or incomplete, is certainly not held in the same regard. A genetic test result tends to be viewed by many, rightly or wrongly, as a far more definitive statement of risk or diagnosis of a disease or condition.

A genetic marker of an individual's susceptibility to serious diseases may also become a part of an individual's health profile possibly far earlier than it might using the conventional strategies, perhaps fifteen or twenty years before such comparable information might otherwise have been surmised.

Results of genetic tests are also not only about the individual involved. Even more than conventional personal health information, they have implications for family members of tested individuals. Regardless of whether a family member wishes to learn the results of a genetic test, the release of revealing information about that family member to a third party may inadvertently trigger a negative series of events with dramatic consequences for that individual and family.

Furthermore, genetic test results may often directly reveal information not only about the individual but his/her family and consideration must be given to those individuals who do not wish to receive this type of information.

Genetic test results have already been sought and used by some employers in the U.S. as a method of screening employees (e.g. Burlington Northern Santa Fe Railroad Company stopped testing employees in April 2001 as part of a workplace discrimination settlement between the railway and the U.S. Equal Employment Opportunity Commission).[34] This practice has lead to speculation about the rise of DNA databanks.

As noted by the recent Human Genome Workshop held by the Department of the Solicitor General Canada, Health Canada, and the Department of Justice:

DNA databanks (storage of genetic information), coupled with the power of informatics, has created a new potential danger regarding invasion of privacy and the potential for discrimination. Employment and insurance are two areas where decisions, based on genetic information, could lead to unreasonable discrimination. While other countries have already taken steps to reduce the potential for genetic discrimination in the areas of employment and insurance, Canada has not yet advanced to the same level.[35]

According to the Privacy Commissioner of Canada, the federal government has stated that Canadians should have a "reasonable expectation of genetic privacy." Yet there is much to be done at both the federal and provincial levels to ensure that appropriate safeguards are in place regarding genetic testing information and addressing public concerns about its use in insurance or employment-related purposes.[36]

Fears about genetic discrimination by insurance companies have been significant in both the U.S. and the U.K. where a number of major initiatives have been undertaken with regard to access to genetic test information.

At its heart, the concern over insurance company access raises the spectre in the minds of some of new categories of uninsurable individuals being created based upon genetically determined risk profiles that attract higher premiums.

Genetic counsellors have also often cited fear of discrimination as a primary reason why some individuals either refuse to be tested or neglect to follow up on the results of genetic tests. There is a similar fear related to prospects for employment or advancement within a particular industry when genetic testing has been undertaken. Addressing these fears in a manner that is fair and open is a challenge that will require much understanding but is an important component of building public trust in genetics.

In both cases of insurance and employment there may be some very valid reasons and circumstances where the use of genetic information is legitimate and necessary. These might for example include measures taken by an employer to protect individuals with susceptibilities from particular workplace risks. However, there needs to be safeguards in place to ensure that when this is the case, that it is by exception rather than the rule and the individual has given fully informed consent.

In Canada, insurers currently do not require genetic testing as a prerequisite to coverage, but access to genetic testing information that has been acquired could be requested by an insurer, as with other aspects of an applicant's medical information.[37]

However, unlike most health histories that document past or present diagnosis, disease and prognosis, some genetic tests are merely predictive and often do not present clear-cut diagnosis. Furthermore, the probability, severity and onset of the predicted disease remains unknown.

Currently, Canada has limited regulation in place regarding access to and utilization of genetic information by third parties. Many jurisdictions such as the United Kingdom and many U.S. states have developed either a voluntary or legislative response to the potential impact of access to genetic information by insurers. (This issue is more fully discussed later in the report.)

Inevitably, as genetic testing becomes more established, all jurisdictions are going to have to examine the need to craft legislation or appropriate alternate mechanisms for establishing limitations on the collection, use and disclosure of genetic information.

2.3 INFORMED CONSENT

In Canada, informed consent is a basic legal and ethical prerequisite of medical treatment, and is fundamental to the provision of genetic testing. In order to consent to treatment, an individual must be capable (e.g., s/he must understand and appreciate the nature of the proposed treatment, including its risks and benefits). The individual must be informed about the medical procedure and consent must be given voluntarily. The individual also has a corresponding right to withhold consent to treatment.

The requirement for informed consent in genetic testing is in most cases a basic prerequisite in order to proceed with testing. With respect to predictive genetic testing, an individual must be informed about all aspects of testing, such as the genetic disorder being tested for, the efficacy of the test, the availability of treatments and the medical and non-medical implications of the test results. Given the complexity and limited accuracy of some current testing technology, it is sometimes unclear how much information health practitioners are required to impart to meet the requirements of informed consent and how much comprehension on the part of the individual is sufficient.

The existing complexity will multiply in the future as tests become available through DNA chip technology and other such approaches begin to allow testing for multiple conditions. The sheer amount of knowledge that will be required to convey the various risk elements escalates with each individual test performed and with it the risk to both the practitioner and patient that something gets left out, the consequences of which may be very significant.

For instance, the highest French court recently awarded damages to a boy for being born, holding that a child can be compensated for being born with a disability or a malformation if the mother was not informed of the risk that could have been evaluated during prenatal diagnosis.[38] This judgement suggests that informed consent in the context of genetic testing is critical. As well, it reflects the expectation that physicians will be knowledgeable about all of the potential genetic tests that a patient would want to know about given his/her condition. As testing moves into more areas and multiple tests are developed the breadth and depth of knowledge that physicians will need in order to ensure that patients are fully informed will become more challenging. At a minimum, the degree of education and training that will potentially be required in certain areas of medical practice will no doubt increase. As demonstrated earlier, the potential liability risks of not having a high degree of up to date knowledge and information conveyed to patients could be high.

Canadian law and policy with respect to informed consent may need to be modernised in the coming years in order to address the new challenges raised by genetic testing. Although most legislation permits implied consent, a decision to be tested for a particular genetic disease or condition may reveal a significant amount of personal information. Many commentators have suggested that consent for genetic testing should be expressly written and limited specifically to the test being performed. Furthermore, healthcare practitioners often find it difficult to reconcile conflicting responsibilities when genetic information reveals important health information about a relative of the individual tested. Guidance should be provided to healthcare practitioners with respect to these potentially conflicting obligations. In an era of predictive genetic testing, redefining what we understand to be "preventing risk of serious harm" will be important as we examine the circumstances in which one individual's genetic information may be released to another without consent.

2.4 DISABILITY

Genetic research and technology has the potential to create new categories of health and "disease", as well as new definitions of "normal". Advocacy groups for the disabled community have long expressed concern about the impact of genetic testing on human diversity. Genetic testing and counselling, it has been argued by some, should not be used solely to eliminate diversity or disability, but to help families to cope with the diagnosis of an inherited disorder, face its implications and make meaningful and informed decisions about their medical and non-medical options.[39] In a presentation to Health Canada on behalf of the Council of Canadians with Disabilities, Dr. Gregor Wolbring noted that "our group believes that society ... lose[s] more than it gains by focusing on predictive genetic tests" and that diagnostic tools should not be promoted which "are only useful to get rid of the diseased, or those with a disability ... before societal safeguards against eugenic abuse are in place.[40]

The challenge for policy and lawmakers is to regulate the use of this technology in order to limit, in both the short and long term, risk of genetic discrimination based on disability. For example, the effects of some genetic conditions or diseases can be mitigated by diet or lifestyle changes, but at present, certain genetic conditions are diagnosed or predicted without the prospect for treatment. Late-onset diseases are often predicted far in advance of the actual development of symptoms or disease. As genetic technology advances, prediction or diagnosis of late-onset diseases, or symptomatic diseases that have no treatment or cure, raise questions about what we mean by "health status" and well-being. Crafting the appropriate balances will not be easy and will go way beyond the sole domain of healthcare ethics.

Improper discrimination on the basis of age, gender, health, disability, sexual orientation, marital or family status is prohibited in Canada. Although it could be argued that genetic information falls under the category of health and disability information, Canada has no legislative provisions that specifically reference genetic discrimination.[41] As a result, Canadians currently may have limited practical protection against the discriminatory use of genetic information except to the extent to which existing protections might be found to apply (e.g. Charter).

"Genetic discrimination is not something that only sick people need to worry about. Every human being is estimated to carry between 5 and 50 flawed genes. Every man, woman and child in America is a potential victim of discrimination."[42]

Moreover, as the mechanics behind molecular genetics are better understood and genetic technology is refined, genetic tests, that we might find almost fantastic today, may be developed. Tests which could target physical or behavioral characteristics such as linguistic or mathematical aptitude, or tendencies toward addiction or depression may be revealed during embryonic development. Ethical, privacy and discrimination issues will proliferate as science and technology progresses.

Canadians need to be engaged in an informed public discussion about the implications of genetic research and notions of health, wellness and disability. All jurisdictions have a responsibility to encourage a social dialogue on the role of genetics in healthcare, a dialogue that goes beyond healthcare providers themselves and engages the Canadian public in discussion about key social questions. Regular dialogue also needs to take place between scientists and those impacted by genetic diseases. **People with disabilities should be represented in discussions between governments and private industry about research and healthcare priorities.**[43]

2.5 TESTING OF CHILDREN

Testing of children for genetic conditions must be undertaken with care. Many commentators have argued that infants and children should not be tested for genetic conditions in the absence of medical/psychological benefits or timely treatment options, as genetic testing early in life may result in discrimination or compromise future healthcare. It is generally accepted that genetic testing for late onset diseases or carrier status information relevant to reproductive decisions should not be conducted on children. Genetic testing, on the other hand, may be advisable where the results of the test may be used to prevent or intervene in the development of imminent disease. Legislative and policy initiatives are required to protect the interests of children with respect to genetic testing.

2.6 MEDICALISATION OF SOCIAL ISSUES

The practical application of new genetic discoveries is often exaggerated and results in medicalisation or "genetisation" of disease, where genes are assumed to be solely responsible for behaviour and health. The relationship between genes and individual traits is still not fully understood, and this view ignores the role of environmental influences upon the genome. While research has suggested that a number of social or psychological conditions may be partly determined by genetics, the balance between genetic and environmental influences remains inconclusive. Genetisation of disease may encourage genetic justification for social issues and decrease individual responsibility for certain actions or behaviour.

3. PATENTS

The introduction of new genetic technologies to detect, prevent and treat illness and disease is accompanied by a collection of social, political, legal and ethical issues. One of the most fundamental and certainly one of the most controversial issues raised in genetics has been that of gene patenting.

The issue of whether or to what extent patents on isolated human genes and DNA sequences can and should be permitted has stirred debate worldwide. Bodies such as the World Medical Association have raised major concerns with the practice of patenting genes and the possible subsequent impact on healthcare (see appendix 2). The European Parliament has debated the issue on more than one occasion with high profile legal battles looming in the background of many of the most positive breakthroughs in biotechnology.

As companies race to identify the specific functions of certain genes and develop and patent inventions related to genetics, Canada and other countries will increasingly be forced to re-examine the efficacy of existing patent systems as they pertain to genetic research and human health. There is a need to ensure that an appropriate set of tools exist to limit possible risks in this area while retaining the incentives for innovation.

In Canada, it is fair to say that the level of public engagement on this topic has, until very recently, been limited in the extreme. Most Canadians are still unaware of the fact that patents are regularly being granted in Canada on information contained in human genes and DNA fragments.

Federal reaction has been slow in joining the debate. Most recently however, the Federal Standing Committee on Health did explicitly address the issue of gene patenting, stating in the December 2001, report on "Assisted Human Reproduction: Building Families" that:

"the Committee is seriously concerned about the patentability of human material. We are deeply disturbed that the Patent Act does not specifically disallow patenting with respect to human genes, DNA sequences and cell lines. Treating human biological components as patentable property is repugnant to many of us. It entails their commodification and paves the way for their commercialization. Given the importance that this Committee attaches to the respect of human dignity and integrity, we urge that patents be denied in relation to human material. There should be particular emphasis on the ethical and social consequence of patenting human material as well as on the implications for the development and availability of related therapies and corresponding costs to healthcare delivery in this country" The Committee in Recommendation 34 recommended that: "The Patent Act be amended to prohibit patenting of humans as well as any human materials."[44]

Another perspective, and one which is perhaps more balanced is contained in the words of Sir Aaron Klug, president of the Royal Society of London:

> **[I]t is critical that the benefits to the public be at least reasonably commensurate to the reward offered by patent protection. Given the enormous potential of the human genome sequence, the granting of broad monopoly patent rights to any portion of it should be regarded as extraordinary–and occur only when new inventions are likely to confer benefits of comparable significance for humankind.[45]**

These words convey the balancing required in the patenting of genes and other human genetic material. The timely caution that the rewards of genetic breakthroughs must be commensurate with the degree of contribution received by society from such breakthroughs. Ultimately it is the terms of the patent contract between the inventors and society that many are urging be examined.

The current patent system in Canada was not, of course, designed to address questions of DNA patenting and the commercialisation of the human genome. While it is true to say that patent law is not, first and foremost, a vehicle for social policy, it is also true to say that patent law must not function in a manner that is in conflict with social policy. It is for this reason that the Canadian *Patent Act* may need to be evaluated and revised to account for a revolution in genetics which the drafters of the Act could never have possibly foreseen.

Canada today has an opportunity and an obligation to examine existing patent law and the frameworks that surround the patent process. This is necessary in order to begin to better achieve a modern and appropriate balance between the public interest in accessing the health benefits offered by genetic technologies and maintaining the economic and commercial incentives that fuel this research.

Increasingly there is recognition that this process is required, but what form should it take? Such a process must be transparent and respect the role of the biotechnology sector but also build in appropriate safeguards for individuals, the Canadian health system and our healthcare providers. Such a dialogue and process is vital if Canadians are to move beyond either ignorance of, or simple opposition to genetic patenting to recognise the role that well-defined patents may continue to play within an appropriate regulatory framework.

3.1 WHAT IS A PATENT?

A patent on an invention may be described, in essence, as a contract between an inventor and society. As reward for the advantage society enjoys from a new or improved product, the inventor receives from society a legally sanctioned exclusive license to make, use, barter or sell that product.

A patent does not give the holder ownership per se, but rather the right to exclude others from making, using, selling or importing the patented invention. In this way, statutory patent rights exist as an incentive to invent, and the ultimate goal of a patent system is to create a business climate that will encourage knowledge, research and development, attract trade and investment and therefore promote economic prosperity.

The broad rights conferred by a patent may be exercised in a number of different ways. At one end of the spectrum, a patent holder may choose not to enforce these rights at all against those who make, use or sell the invention. On the other hand, a patent holder may decide to either provide the product or service exclusively, or to grant an exclusive license to another provider. Under this approach, the patent holder retains a high degree of control over pricing and other aspects of distribution related to the invention.

The patent holder may also choose to use a broader licensing strategy by licensing the invention to a small number of distributors with a non-exclusive license. With respect to a patented genetic test, this arrangement would allow the patent holder to control certain aspects of how the test is conducted and delivered, including future access to the samples for the purposes of research. Another approach would involve granting a non-exclusive license to use the invention upon payment of royalty fees. In this instance, a patent holder can limit the availability and accessibility of the invention by setting higher fees for use.

While the existing framework offers a range of approaches to patent holders, and thereby has a degree of flexibility to accommodate different business models, it does not contain within the patent approval process clear and easy procedural processes for opposition. Furthermore, the legal protections which do exist for such things as research, public non-commercial use and medical use are far from clear.

In most countries, patent priority is based on the "first to file" principle—the US is the only country to use the "first to invent" principle. The criteria for patentability of an invention varies from state to state, but is determined by reference to variations on the following four criteria:

a) the invention must be useful in a practical sense, and a useful purpose must be identified in the application.

b) the invention must also be novel, in that the product claimed is /was not known, used, or available in the claimed form before the filing of the patent application.

c) the invention must be "non-obvious", and not simply an improvement that is easily made by someone trained in the relevant area.

d) the invention must be described in sufficient detail to allow someone skilled in the relevant field to use it for the purpose stated in the application.

An invention is not patentable if it is any of the following:[46]

- a discovery (e.g. something that was not the result of ingenuity);
- a scientific theory or mathematical method;
- an aesthetic creation, such as literary, dramatic or artistic work (these can only be copyrighted);
- a scheme or method for performing a mental act, playing a game or doing business;
- the presentation of information or a computer program (these can only be copyrighted);
- a method of treatment of the human or animal body by surgery or therapy (e.g. a doctor cannot patent a new way of performing an appendectomy or a balloon angioplasty);
- in some jurisdiction this restriction may also include a method of diagnosis (included as an allowable exception in recent international agreements).

Many of these exceptions are provided through either the *Patent Act* or through procedural guidelines issued by individual patent offices. New technologies do not always fall clearly within the definition of invention, and interpretation by patent examiners and the courts continually redefines the boundaries of patentable subject matter.

Each country enacts its own patent legislation, and an inventor must apply for a patent in each country where s/he wishes to obtain protection. However, there are a number of international instruments that limit or expand upon the content of these laws, the aim of which is to ensure fair competition among international players with respect to inventions and patent protection.

a) The Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPs) is a creation of the World Trade Organisation, and was created from the Uruguay Round General Agreement on Tariffs, and Trade (GATT). This sets out the minimum standards of protection for intellectual property to be provided by each party to the agreement.

b) The North American Free Trade Agreement (NAFTA).

c) The Paris Convention for the Protection of Industrial Property.

d) The Convention on Biological Diversity.

These documents impose limitations upon:

- the types of inventions that can and should be protected;
- the types of tests that may be employed by a country to determine patentability;
- the extent of any limitations that may be placed upon the scope of the patent by the granting country; and
- the ability to permit people other than the patent holder to use or make an invention without permission.

Most patent legislation also incorporates various remedies to address inequitable or unfair use or abuse of patent rights. Remedial options range from granting intervenor status to challenge an invention, the inclusion of a public order/morality clause that provides a ground for refusal of a patent, or compulsory licensing provisions that require reasonable licensing agreements under certain circumstances.

3.2 CAN GENES BE PATENTED?

In general, *raw products* of nature are not patentable. A patent is granted to the entire process of discovering and isolating in the laboratory certain strings of DNA that were not obvious before, rather than to a gene as it *exists in nature.*

In order to patent a gene, a sequence, or other similar material, an inventor must identify or modify the novel genetic sequences and specify the product of the sequence and how it functions in nature. This specification must enable others with similar skills and knowledge to use the sequence in the same way for the purpose claimed in the application. In this respect, where the DNA products are isolated, purified or modified to produce a unique form not found in nature, they may be considered patentable. In practice, however, the utility of the DNA product is often quite vague and numerous patents have been granted in the U.S. and elsewhere for genetic sequences whose full or even partial use was not known at the time of the patent being issued.

3.2.1 HOW DID WE GET HERE?

In a 1980 case, *Diamond* v. *Chakrabarty*, the U.S. Supreme Court determined that a genetically engineered bacterium was patentable.[47] According to the court, the relevant distinction to be drawn was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions. Some analysts, however, criticised the Supreme Court ruling on the Chakrabarty case on the grounds that the loose interpretation of "ingenuity" and "novelty" given by the Court would set a dangerous precedent for future patents. This case opened the door to the patenting of living organisms or innovations developed from living organisms.

As technology increased in sophistication and the commercial application of biotechnology became more common, biomedical researchers and their funding agencies increasingly looked to patents to protect their commercial interests. For many players in the biotechnology sector, the identification of human genes and DNA sequences is undertaken as a prelude to either pharmacologic or technological development.The patent is seen as one component of an overall business framework.

This is an understandable feature of the biotechnology industry and the need to protect invention. However, taken to an extreme, this process has led to in some cases to speculative patenting, where patents have been sought and in some cases granted, where the full utility of a gene is as yet unknown, but simply suspected.

Such approaches return us to the concept of the patent as a contract between society and the inventor and the need to revisit, especially in the case of genes, the precise terms of that contract. This debate and discussion about the terms of the contract underpinning a gene patent has sparked debate worldwide. A key milestone in the move to gene patenting in Europe came in the late 1990's with the *European Directive* on the Legal Protection of Biotechnology.

3.2.2 EUROPEAN DIRECTIVE ON THE LEGAL PROTECTION OF BIOTECHNOLOGY

In 1998, the European Parliament concluded ten years of debate by approving the European Directive on the Legal Protection of Biotechnology. Although controversial, the Directive attempted to clarify and standardize patent laws for biotechnology. The Directive includes a provision preventing "commercial exploitation [of biotechnology which] would be contrary to public order or morality." The Directive thereby attempts, in however a limited fashion, to incorporate ethical principles into the discussion of patent law.

The European Directive on the Legal Protection of Biotechnological Inventions

The Directive aims to harmonise the national laws of Member States and to clarify the legal framework for patented biotechnological inventions. The Directive differentiates between discoveries and inventions, defines the scope of protection offered by biotechnological patents, and creates the option of obtaining non-exclusive compulsory licenses.

With respect to human genetic material, the Directive states that the human body is not patentable at any stage of its development and neither are simple discoveries of its elements. However, an element isolated from the human body, or otherwise produced by means of a technological process, may constitute a patentable invention. This includes the sequence or partial sequence of a gene, even if the structure is identical to that of a natural element. The Directive also states that the industrial application of a genetic sequence or part of a genetic sequence must be disclosed in the patent application, and the examination of a patent application of this nature should be subject to the same criteria of patentablity as any other area of technology.

The enactment of the Directive was not without controversy and criticism. In France, the Justice Minister has disputed the patentability of genetic material, and France has introduced legislation to implement all aspects of the Directive except for the provisions relating to gene patenting. In a similar spirit of protest, the Netherlands, Norway and Italy filed a challenge to the Directive to the European Court of Justice. However, the European Court of Justice dismissed the challenge on October 9, 2001.

3.2.3 PATENTS ON LIFE FORMS

Patents on life forms have been permitted in Canada since 1982, when the Commissioner of Patents granted two patents on micro-organisms.

In the *Abitibi* [48] case, a patent was granted for a yeast culture used to purify effluent from the manufacture of wood pulp. The Commissioner held that when micro-organisms are prepared in large numbers, any measurable quantity will possess uniform characteristics and properties and will therefore be patentable. Similarly, in *Connaught*[49] *Laboratories*, a patent was granted for a culture of a bovine cell line useful for the production of insulin.

In 1988, the Patent and Trademark Office in the United States (USPTO) extended patent protection to higher life forms and allowed a patent on the "Harvard Mouse", a mouse genetically engineered to be susceptible to cancer for use in medical research. The Canadian Intellectual Patent Office (CIPO), however, rejected the application and the applicant, Harvard College, appealed the decision. The Canadian Federal Court (Trial Division) affirmed the Commissioner's decision, but the Federal Court of Appeal allowed the College's appeal in 2000. This latter decision broadly interpreted the definition of invention in the *Patent Act* and ruled that it included genetically-modified, non-human mammals. Leave to appeal to the Supreme Court of Canada was granted in June 2001, and the Court is expected to hear the case in Spring, 2002.

In Europe, the European Patent Office granted a patent for the genetically modified mouse in 1992 despite considerable criticism. More than 300 organisations protested the decision on ethical and environmental grounds stating that the mouse posed unacceptable risks to the environment, and that the patent violated public order and morality since genetically engineering an animal that was predisposed to suffer was contrary to morality. This protest led to the filing of an opposition to the patent in 1992, and it took until November 2001 for the EPO to finally decide that the patent was valid but should be restricted to rodents.

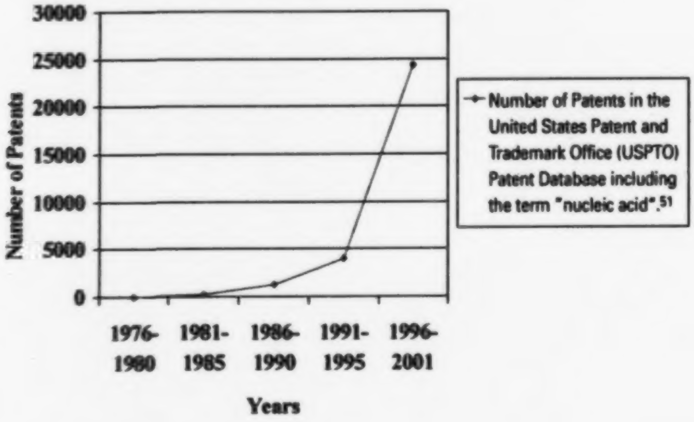
3.3 SCOPE OF GENE PATENTING

Since the *Chakrabarty* case in the U.S., patents have been issued on entire genes and their protein products where the functions of these are known. More recently, patents have been sought on sequences of DNA that are less than a whole gene, and the patentability of these SNPs and ESTs is not yet fully clear.

Further, where a patent is sought for a DNA fragment, it is unclear whether a second patent may be issued for a larger fragment that contains the original fragment. This issue arises in the patenting of expressed sequence tags (ESTs). ESTs are not complete genes but fragments of genes, and in many cases are patented without a description of the exact location of the original gene on the chromosome and/or its biological function. This lack of specificity has made the patenting of ESTs controversial among some scientists and is one for which there appears to be good reason to express caution.

A similar issue occurs with single nucleotide polymorphisms (SNPs). SNPs are DNA sequence variations that occur when a single nucleotide in the genome sequence is altered. In the Human Genome Project, SNPs are used as markers to locate disease genes. Variations in DNA sequence can have a major impact on how humans respond to disease, environmental insults such as bacteria, viruses, toxins and chemicals, and drugs and other therapies, and SNPs. Therefore quite useful in biomedical research and for developing pharmaceutical products or medical diagnosis. For this reason, many have argued that SNPs and ESTs and other DNA research "tools" should not be patentable.

According to one study 9,000 patents have been issued on genes, gene sequences, and gene fragments, and tens of thousands of applications are awaiting consideration. [50]



3.3.1 STEM CELLS

Stem cells are cells with the potential to develop into many different types of tissues and organs. Human stem cells can be derived from different sources. The sources are adult stem cells, fetal stem cells, embryonic stem cells and umbilical cord blood.

This year a U.S. research foundation and a U.S. commercial company reached a patent licensing agreement on embryonic stem cell types and technology.[52] While the research foundation owned five of the 72 stem cell lines eligible for use in U.S. federally funded research, the commercial company held the licensing rights to some of the technologies used to derive, culture and maintain those cells.[53]

The agreement gave exclusive rights to the commercial company to develop products from stem cells derived from nerve, heart and pancreas cells and non-exclusive rights to the use of blood, cartilage and bone cells. The agreement also allows academic and government researchers use of the patented technology without a licensing fee as long as the work is for research rather than product development.

While this arrangement seems to prevent monopolistic rights from accruing on stem cells and preserves not-for-profit research, stem cell patents promise to raise a new host of issues. Stem cells can theoretically be developed into a myriad of tissue and organs and the implications of patents on stem cells require further analysis. To what extent does a patent on a technique for cultivating human blood or liver cells defacto become a monopoly on their artificial production? **The commercial company mentioned above has already derived heart, nerve, pancreas, bone, liver and blood cells from the stem cells and has filed for patents on the techniques used in their development.**[54]

The example above raises a host of questions and issues regarding the scope of stem cell patents. Since stem cells have the potential to be developed into tissues and organs, the potential use of them for curing and treating many conditions and diseases is enormous. The patenting of stem cells may well mean that exclusive royalty fees will have to be paid in the future for replacement organs and tissues, developed in this manner, raising significant implications for publicly funded healthcare systems.

3.3.2 SNP CONSORTIUM

In 1999, ten large pharmaceutical companies and the U.K. Wellcome Trust, a not-for-profit, non-governmental organization, announced the establishment of a non-profit foundation to find and map 300,000 common SNPs and to make the information publicly available.[55] The SNP Consortium Ltd. was founded on the premise that genetic research related to SNPs is accelerated when research findings are freely available to all researchers and companies. The initiative also aims to avoid duplication of effort and to prevent companies from developing private maps that would tie up large areas of the human genome with patent claims. The research generated by the consortium is maintained on a free, public database at the National Institutes of Health in the United States.

In a speech to the Rideau Club in February, 2000, Dr. Michael Levy of Glaxo Canada (now GlaxoSmithKline), pointed to the SNP Consortium as an important means of keeping genetic information in the public domain.[56] Furthermore, he said, "Competitive advantage for us lies in being able to use this [genetic] knowledge to turn it into important new medicines." His sentiments have been previously echoed by the various members of the SNP Consortium. The SNP Consortium is viewed by its members as an important means of preventing "patent stacking" and promoting collaborative research in the development of pharmacogenomics.

For the pharmaceutical industry, patent protection is naturally viewed as vital to the production of new drugs and interventions. The Consortium has however adopted an approach through the SNP project that treats SNP information (non-patented) as primarily an informational input freely available and yet, still providing a vital contribution to downstream product development.

3.4 ISSUES IN GENE PATENTING

The patenting of biotech inventions in general has always attracted considerable debate. Intellectual property advocates argue that without exclusive rights to the fruits of their labour, inventors would not have any incentive to invest in research and development. In the search for patentable innovations, research is forced into new, unexplored areas, and scientific secrecy is reduced as all researchers gain access to the research upon publication of the patent. In the area of health science, many argue that patents encourage the development of new applications for healthcare resulting in new diagnostic and treatment options.

However, others have argued that the current patent system, in certain circumstances, may allow certain patents which could hinder further research and could interfere with innovation. The argument has also been made that the patenting of diagnostic technologies could carry the risk of possibly limiting accessibility to medical treatment.

The knowledge generated by genetic research promises to greatly improve human health and the delivery of healthcare. However, the key challenge for any jurisdiction is how to carefully balance the public interest in access to the discoveries and inventions that result from genetic research, with the economic and commercial incentives that fuel much of this research.

The sharing of scientific knowledge via a patent occurs when an invention has been patented and therefore published. Because patent applications remain secret until granted, companies may work on developing a product only to find that new patents have been granted along the way, with unexpected licensing costs and possible infringement penalties. In fact, the novelty requirement of patent law requires that inventors keep their inventions secret for a certain period of time.

This element of secrecy in genetic patents can have an impact in the laboratory. One 1997 study found that the pressure to obtain a patent may sometimes create an atmosphere of secrecy among researchers. [57] This survey of U.S. life science researchers suggests that most researchers with a commercial motivation or an industry affiliation tend to quite naturally withhold the results of their study until after the patent application is filed.

The peculiar nature of gene patenting also raises a number of concerns which are specifically related to the stage of our knowledge of the human genome and the stages of development of genetic technologies. Genetic research is, despite the progress made to date, still in its relative infancy and granting patents on genes on the basis of one utility may, some have argued, encourage premature commercialisation of the technology and discourage further research into another equally useful or more efficient utility.

A broad-based patent on a certain gene or gene sequence and its diagnostic use may also introduce something of a disincentive for other researchers to develop a new, potentially more accurate test which examines the same gene.

Even if subsequent research does result in the development of more accurate or effective diagnostic or treatment methods being developed, or even an alternative but related utility being identified as some genetic material performs multiple or changing functions, the original patent holder (depending on the breadth of the patent issued) may enjoy exclusive rights to the use of the genes for these purposes. There are few good analogies in more traditional areas of patenting to the potential scope and breadth of control that a holder of a gene patent technically holds over other innovations in the same field.

This issue was highlighted in the mid-1990s when Human Genome Sciences applied for a patent on the CCR5 gene, which produces a receptor cell that binds protein molecules to the surface of a particular cell.

The patent application covered the gene and its protein and the fragments of DNA used to locate the gene, as well as details related to the chemical components of the gene, and potential applications of this knowledge. Despite the fact that independent researchers at the National Institutes of Health in the United States subsequently discovered that the gene functions as a receptor for the entry of HIV into the human body, the patent was eventually granted to Human Genome Sciences. Furthermore, Human Genome Science's patent on the gene permitted it to use the gene for any purpose, and therefore profit from the later discovery. This patent has resulted in considerable control over the commercial development of a new class of AIDS drugs, even though the role of CCR5 in HIV infection was unknown at the time of filing. [58, 59]

"Any scientists who begin using it (CCR5) now might have to pay HGS. Such a license may amount to something in the area of 10% of a drug's future revenue"[60]

One U.S expert summed up the situation as follows:

"In effect, this is like patenting a hydroplane with a propeller and then claiming that the patent covers airplanes because both have propellers, wings for lift and cut through air at some level. Such theoretical patents are overbroad and in effect do not accurately cover what was actually invented, if anything at all and such patents provide a continuing basis for extensive litigation, thereby delaying or impairing commercialization of such research (e.g. new therapies, diagnostics)[61]

In another example, HIV II rapid test kits, currently available in many jurisdictions around the world where patents on HIV II do not exist, are not yet available in the U.S. The U.S. Centre for Disease Control has expressed concern over what has been reported as the use of a biological patent as a mechanism to restrict access to newer cheaper technology by a patent holder with investments in more traditional testing techniques.

Unlike the invention of the mousetrap, the potential consequences of gene patents could yet prove to raise significant access issues within healthcare, this would be especially significant if access to genetic testing and work on future diagnostic procedures using the same material is either restricted or subject to hefty licensing or royalty fees.

Genetic discoveries usually occur from the top down; that is, the discovery of the gene often precedes discovery of its constituent parts, proteins and functions.

Future discoveries and inventions related to smaller parts of the genome may, depending upon the nature of the gene patent and the approach taken to enforcement, be made contingent upon licensing and royalty agreements based on existing patent claims on the larger pieces of the genome.

Many researchers have expressed concern about the extent to which patents on partial gene sequences may impose dependency or "reach-through" to subsequent patents with full length DNA sequences and functional genetic data. The "reach-through" license agreements give the owner of a patented invention used in early, or "upstream", research licensing rights in subsequent, or "downstream", research, and the effect is stifling where the potential multiple licensing agreements can serve to block future research endeavours.

Each upstream patent, if exercised to the fullest extent could, in effect create a tollbooth to subsequent research and development, potentially adding to the cost and slowing the pace of downstream biomedical innovation.[62, 63]

The possible stifling effect of gene patents on research was highlighted in a recent pilot study conducted by Mildred Cho at Stanford University in the United States. This study found that 25% of U.S. university and commercial laboratories surveyed refrained from providing genetic tests, or continuing carrying on with related research due to either a fear of patent infringement or to insufficient funding for the required royalty or licensing fees. [64]

Additionally, 48% of laboratories studied decided not to develop genetic tests based on patented genetic material. This study emphasises that the discovery of human biological products cannot be viewed as an end in and of themselves, but that effective regulation must also examine the manner in which this knowledge is applied in society and the degree to which the patent acts as intended, which is as a tool for future innovation and development.

Genetic discoveries and inventions differ therefore in several important respects from other types of research and development. Traditional arguments in favor of the patent system may not adequately justify, without certain qualifications and limitations, the sorts of broad patents on biological materials that have been issued in recent years.

Inventions such as the light bulb, the mousetrap or other household commodities that promise convenience are typically ends in themselves, and patents are relied upon to encourage innovation and investment for their development and improvement. Genetic research, on the other hand intersects, at least in part, with the common goal of improving human health and well-being.

In a similar way, many aspects of clinical research and development have not been discouraged by the lack of patent protection on such things as surgical techniques.

There is also a danger that has been expressed by some that the commercialization of genetic information and the potential imposition of twenty-year monopolies could, through restrictive costs or licencing, lead to inequitable access to medical applications of genetics according to the ability to pay. This may have the potential in the long run of being true not simply within countries, but between countries.

What we have witnessed in terms of the grueling debates regarding the rights of African countries, among others, to access patented HIV medications affordably , we may yet witness again, some years from now, in future debates with regard to patented genetic interventions. This is a serious concern.

Perhaps the most significant difference between genetic discoveries and more traditional inventions lies in the breadth of the patent itself. Genetic material not only is a chemical having a chemical function, but, together with the proteins the genes produce, also carries the sole source of information about one component of a particular person's genetic makeup.

Patent law in Canada is designed to balance the interests of different competing commercial users of a technology, and it was never intended to prevent access to basic information. In fact, the *Patent Act* and patent law in general seek to prevent the award of patents on information, and it is this concept that underlies the exceptions to patentability, described earlier.

In order to remain consistent with current patent system, some have argued that gene patents, therefore, should focus on the gene solely as a chemical compound rather than primarily on the information contained within the gene or on the gene as a whole. While such an approach may be complex, it requires consideraton.

3.5 CONSEQUENCES FOR HEALTHCARE

In some ways it may yet be too early to fully outline the possible consequences for healthcare of gene patenting. While many in the international medical community have voiced concerns and speculated as to the possible consequences for medical practice, in reality, we have only very recently seen the first impacts of enforcement of broad genetic patents begin to play out in the Canadian healthcare system. Perhaps little will happen and isolated cases will be resolved. Perhaps existing regulatory and oversight provisions will prove adequate to preventing any potential abuses of the system.

We could certainly sketch a rough outline of some of the possible outcomes of gene patenting. It is likely that the health sector will face more exclusive licensing arrangements, whereby requirements are set down by the patent holder to ship samples to a specialized facility out of province or potentially out-of-country. We can also anticipate that the payment of royalty fees for new tests will expand considerably, given public interest in and demand for new tests which will become available. These costs have the potential of escalating rapidly.

Beyond these obvious factors other changes are less clear. For example, to what extent will clinical practice be compromised by exclusive testing agreements effectively limiting the types of tests that can and cannot be performed using a patented gene or gene sequence? Perhaps as importantly, how will better and cheaper diagnostic innovations come on stream when their very development may also be limited by licensing conditions imposed by an original patent holder on the genetic information?

The questions become even more complex as we anticipate a world where many tests may become available over the internet and whether either directly or through its growth in other countries, direct-to-consumer marketing in genetic testing begins to take hold. The current framework of counselling and clinical advice is a constitutive part of genetic testing in Canada today. This structure of care could also face disruption as tests become increasingly available in kit form or at a distance or as the sheer volume of tests stretch counselling capacity to the extreme. As the centre for Health Economic Policy Analysis (CHEPA) noted in a recent report:

> **As the breadth of genetic testing services expands to include the promotion of tests for common disorders, the potential demand induced by marketing may outpace our capacity to offer genetic counselling necessary for informed consent (Collins 1999). Moreover, some genetic testing sevices may be marketed before effective preventative treatments are available.[65]**

There is also some risk that without appropriate safeguards, the commercial considerations of genetic patenting could also result in genetic tests being offered commercially too early, before the results of testing can be properly interpreted, evaluated and used. It is important, therefore, that post-marketing studies are conducted so that outcomes for health, family and social ramifications are fully understood.

As a society, we can approach the question of impact of gene patenting in many ways. If the patent is indeed a contract between the inventor and society, perhaps the more appropriate way to answer the question about the impact of gene patenting on healthcare is to state that the impact will ultimately be what law and society allow the terms of that contract to be.

It is precisely because of the contractual nature of the patent that society has the responsibility to articulate clearly the meaning and boundaries of that contract.

3.6 PATENT REFORMS

Three choices appear available to Canadians with regard to gene patenting. We could, as has been recommended to the Federal Minister of Health in December 2001 by the Federal Standing Committee on Health, simply recommend the prohibition of any patents on genes or DNA. This approach has the advantage of being clear and would certainly fit with where many Canadians instinctively feel the law should be. By taking this approach however, we would risk losing much.

The protections offered by patents are perceived as a fairly fundamental cornerstone in protecting the rights of the inventor in our society. In the genetics field, patents are seen by many as a method of recognising the valuable contributions and investment made by the biotechnology sector. In Canada, these patent protections also enable us to compete in an international context.

We could, on the other hand, ignore the Standing Committee on Health and simply wait and see what the impact of gene patenting will be on healthcare, on research, on clinical practise and service delivery. This approach has the advantage of maintaining a status quo. It has the possible disadvantage however of effectively disengaging, of risking not developing the tools and mechanisms in advance to anticipate change. Already, Canada lacks a number of the protective mechanisms currently in place in the patent laws and oversight processes of other jurisdictions. Staying in place may, in effect, be tantamount to moving behind.

The third option available to Canadians is to recognise that the speed of genetic discoveries and the promise of genetic medicine require that the federal and provincial governments develop forward looking solutions. This approach would recognise that genetic information and genetic inventions differ from other types of inventions, and that the patent protections for these inventions and the processes within which they are excercised should appropriately reflect these differences.

Ultimately patent law and policies with respect to genetic patents need to be amended in order to carefully balance public interests with economic and commercial incentives.

In November 2001, the Canadian Biotechnology Advisory Committee (CBAC) released its interim report "Biotechnology and Intellectual Property: Patenting of Higher Life Forms and Related Issues."[66] The report recommends further study on the effects of biological patenting on the healthcare system, such as incentives or disincentives of patents on healthcare, the availability of patented inventions to the healthcare system, and whether these patents suggest a need for differential treatment in patent law. Much of this is wise advice.

The CBAC also suggests that the *Patent Act* should be amended to include a clear research and experimental use exception. This exception would preclude infringement proceedings for the use of a patented process or product for private or non-commercial study, for research on the properties of the patented invention, for improvement upon the patented product or process, or for the creation of a new product or process. This exclusion from liability would address many of the concerns raised by researchers and clinicians respecting the efficacy of the patent system in relation to gene patents, and the accessibility of genetic health technologies to Canadians who would benefit from this type of care.

The CBAC also recommends that the Canadian Intellectual Property Office (CIPO) develop and publish interpretive guidelines concerning biological materials which include the criteria for issuing a biological patent, how traditional knowledge is to be described as prior art, and the process and timelines for application. The CBAC also suggests that an "ordre public" or "morality" provision be included in Canadian patent law to provide an opposition procedure, either as an amendment to the *Patent Act* or within CIPO guidelines.

The ordre public or morality provision provides the ability to withhold patents on a case by case basis. Many of the patent systems in the world include this provision in their patent legislation, with the exception of Canada and the United States. Most notably it is also a feature of the *European Unions Directive on the Legal Protection of Biotechnology*.

The European Community already therefore explicitly recognises that some inventions violate morality. These processes might include processes to clone human beings, to modify the human germline, to use human embryos for commercial purposes and altering the genetic identity of animals to cause suffering without a substantial benefit to humans. As stem cell research develops we must ask whether a monopoly on the method to create a new human liver or other organ would not be an affront to Canadian values and morality.

In addition to these recommendations, other appropriate mechanisms exist to address the ethical and social concerns attached to gene patenting without undermining incentives to invest or diminishing Canada's role as a leader in the field of biotechnology. (e.g., appropriate oversight, separate legislation).

3.6.1 SUMMARY OF RECOMMENDATIONS:

Building on the work of CBAC and consistent with a goal of balancing the interests of the healthcare system with the role played by the biotechnology sector in Canada we recommend that the following approaches are worthy of serious consideration by the federal government in the area of gene patenting.

3.6.1.(A) CANADIAN INTELLECTUAL PROPERTY OFFICE (CIPO)– DEVELOPMENT OF POLICIES AND TRAINING

1. Develop Guidelines and Procedures for Biological Patents

As an immediate measure, the CIPO should develop publications and update its procedural manuals to address issues related to the patenting of biological materials. Current standards of "novelty, non-obviousness and utility" are not yet well adapted to biotechnological inventions. Furthermore, there are no clear patent office guidelines. Appropriate interpretive criteria should be made available to patent examiners who determine whether certain biological inventions fall within the definition of patentable subject matter. Additional training materials should also be provided to patent examiners that focus specifically on biological patents.

The United States Patent and Trademark Office (USPTO) has published a revised set of guidelines to be used by office examiners in their review of patent applications for compliance with the utility requirements of American patent law. These guidelines are used in conjunction with other resources and materials provided to U.S. patent examiners. Training materials have been printed to accompany the guidelines, and provide direction to the implementation and interpretation of the new utility requirements. The USPTO also provides handbooks and manuals relating to classification of inventions and special consideration required for particular types of inventions, such as computer related inventions. This material is available online at the web site of the U.S. Patent and Trademark Office.[67]

The Canadian Intellectual Property Office[68] provides similar materials on its website; however, an updated manual relating to biological materials does not appear to be available. The current Manual of Patent Office Practice came into force on October 1, 1996, and amendments relating to contacting the patent office (Chapter 1) and protests and filing of prior art (Chapter 18) came into force in early 2000.

2. Tighten Utility Requirements for Biological Patents

The U.S. Patent and Trademark Office (USPTO) also revised its utility guidelines[69] in early 2001 to develop definitive utility standards for the patenting of genes and gene fragments. These amendments require an inventor to assert a "specific and substantial utility" that a person of ordinary skill in the art to which the invention pertains would consider credible. A utility is "specific" when it is particular to the subject matter claimed, and a utility is "substantial" when no further research is required to identify an immediate benefit. For example, a fragment of nucleic acid that has a claimed utility as a gene probe or chromosome marker must also identify the particular gene or chromosome target. Furthermore, a patent on the use of the fragment for the purpose of locating these targets may also require linkage to a specific disease or application.

Through this process, the USPTO rejected an outright prohibition on the patenting of this type of material, and instead focused on tightening technical procedures to address concern surrounding these patents.

The USPTO has stated that "throw-away utilities" would not meet the specific or substantial utility requirements:

> **Using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilitites that would not pass muster as specific or substantial utilities under 35 U.S.C. 101. This analysis should, of course, be tempered by consideration of the context and nature of the invention. For example, if a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.** [70]

3. Clarify Definition of "Patentable Subject Matter"

The CIPO should also revisit its criteria for patentable subject matter and develop standards for utility for applications related to biological patents. The utility doctrine can be used to restrict the patenting of fundamental genomic "concepts" and genetic research tools. Biological patents should only be granted for specified uses and narrow applications. The scope of the patent should be limited solely to these specific claims. For instance, where a useful function of a gene can be demonstrated, it may be reasonable to allow a patent on the gene or its product in connection with its use. This additional rigour would at least in part address the problem of "patent stacking" and the anomalous results that flow from a later utility for a patented gene.

This approach would also address the concern about the efficiency or effectiveness of existing patented technologies. Patent claims on a gene sequence that cover uses for all diagnostic innovations in the future are not in the public interest or in the interests of the promotion of a competitive market in diagnostic testing. Maintaining the status quo in this regard may actually serve as a disincentive to the improvement of existing products and the development of larger numbers of commercial applications. The concept of improvement is fundamental to the patent system and one in which there appears to be something of a potential dissonance between certain biological and non-biological patents.

3.6.1(B) AMENDMENTS TO THE PATENT ACT

Despite the options available to the CIPO in respect of training and the development of guidelines, the *Patent Act* should be amended to specifically address the unique nature of biological patents. Gene patents differ significantly from their non-biological counterparts, and patent law must reflect this difference.

4. Define the Scope of Gene Patents

As discussed, the effect of fully enforced, broad scope gene patents may challenge certain principles of patent law by in effect patenting genetic *information* rather than simply genetic inventions, products or utilities.

To remedy this problem, the scope of patents over genetic material may need to be more rigorously defined to separate the chemical or structural nature of genetic material from its informational content. Patents should only prevent the making, using, selling, and importation of genetic material when that material is used as a chemical, but should not unduly limit access and use of the particular information content of a naturally occurring sequence, regardless of whether the sequence is being used in a natural or artificial form.

Focussing the scope of gene patenting would still permit a patentee of genetic material to prevent others from making, selling, using, or importing commercially reproduced copies of that material to be used in an industrial setting. However, reproduction of the same genetic material could not be prohibited by the patentee when it was used for healthcare purposes related to an individual. Given this situation, it is imperative that the federal government specifically incorporate regulation making abilities respecting the scope of gene patents into current patent legislation.

5. Clarify "Experimental Use" and "Non-Commercial Clinical Use" Exceptions

In order to address potential impediments to research caused by broad gene patents, the "experimental use" exemption in the *Patent Act* should be clarified. Section 55.2 of the *Patent Act* states that it is not an infringement to make, construct, use, or sell a patented invention in order to conduct research aimed at satisfying federal or provincial regulatory requirements with respect to the sale of a product. This provision is primarily aimed at the generic pharmaceutical industry and has recently been upheld by a dispute-resolution panel under the World Trade Organisation. A second exception has been judicially created, and permits research with a non-commercial end on the subject matter of the patent. As the law currently stands, however, it is unclear whether a researcher conducting research using a patented invention could successfully be sued where that research has the *potential* in the longer term to result in a commercial product.

At the present time, neither of these exceptions is broad enough to assure that molecular biologists will not be sued for patent infringement respecting research that may ultimately have a commercial end. This uncertainty raises the possibility of the abandonment of research projects and product development. In order to ensure that the development and improvement of genetic diagnostic and screening tests continues, researchers must be confident that their work, if appropriately pursued, will not result in a patent infringement suit or risk of such suit.

As the CBAC notes, the *Patent Act* should be amended to specifically include an experimental use exception that protects private or non-commercial study on a patented invention, or research on the patented subject matter to investigate its properties, to improve upon it, or to create a new product or process. This amendment should also be extended to non-commercial clinical use.

6. The Ordre Public or Morality Clause

In most countries, intellectual property law is not currently designed to consider social policy considerations. It must, however, have some capacity not to run counter to social policy. In the United States and Canada, the patent office has no explicit authority to refuse a patent application on the grounds that it may be deemed to be contrary to ordre public or morality.

European countries, on the other hand, explicitly incorporate an ordre public or morality clause in their patent legislation that provides that inventions that are against ordre public or morality will not be considered eligible for patent protection. However, The European approach is not without difficulties. In Europe, the morality clause is applied, in the first instance, by patenting examiners who do not necessarily have expertise in ethical matters, and are therefore uncomfortable in applying the clause.

One of the central themes of this report is the distinct ethical and social issues raised by DNA patents. While it is difficult to legislate the rapid progress of science, the amendment of the *Patent Act* to include an ordre public or morality clause would operate to provoke sober second thought for more contentious patent applications. The patenting of stem cells, for instance, promises to be controversial because the essence of stem cells are growth and development of raw cell material into many types of human tissue and organs.

The federal government should consider the modalities of amending the *Patent Act* to include an ordre public or morality clause. Specifically, the provisions should address the bases upon which a patent can be challenged for contravention of the clause, the body that should make determinations regarding the application of this clause, and the remedial powers that should accompany the determination. In particular, the federal government ought to consider establishing a body separate from the patent office, comprised of experts in science, ethics and competition law to review patent applications for this purpose. In other words, the process of issuing patents would be separate from the process of reviewing patents for compliance with particular moral standards. A specialised review body that exists apart from the patent issuance process would overcome the reluctance faced by the European patent examiners to make pronouncements based on ethical or moral criteria. The review body would have the power to suspend the operation of the patent, as well as to lift the suspension as offending aspects of the application are remedied.

7. Replace Methods of Medical Treatment Exclusion

Through court decisions, Canada has decided not to provide patents over methods of medical treatments. This is consistent with Canada's international trade obligations, as signatory countries to these documents are entitled to withhold patents over methods of medical diagnosis in addition to methods of medical treatments.

Under current law, a method of medical treatment only includes *in vivo* procedures, or procedures that are carried out inside the body. The exception does not apply to devices or procedures carried out *in vitro*, or exclusively outside the body. Given the realities of contemporary biotechnology, this is a theoretical distinction and practicably difficult to maintain. Many medical procedures involve elements that are carried out both within and outside the human body. Given this mixture of *in vivo* and *in vitro* procedures, patentees could, in effect, obtain patent protection that would prevent medical practitioners from carrying out medical activities without permission.

The United States, on the other hand, does not exclude methods of medical treatment in its patent law, but U.S. law does provide that a patentee cannot pursue a medical practitioner or the medical facility for the provision of patented medical services to a patient[71]. The adoption of this approach by Canada, with an extension to cover diagnostic procedures, would address the clinical concern about access to genetic technologies for the purposes of healthcare. The federal government should, therefore, amend the *Patent Act* to explicitly replace the methods of medical treatment exclusion in patent law with a provision stating that a patentee cannot bring an action for infringement against a medical practitioner for providing medical services, including both treatment and diagnosis, to patients. The liability protection should extend to physicians, nurses, pharmacists, health technicians, and other healthcare practitioners, as well as their medical facilities. This approach while providing protection would still allow the full patenting of genetic testing technologies.

8. Introduce an Opposition Process

Given the overburdening of the patent offices, patents may be wrongly issued. While the *Patent Act* currently provides for a process of re-examination with respect to previously undisclosed prior art and a process to challenge an issued patent before the Federal Court, these mechanisms are insufficient to protect Canadians. The re-examination process is overly narrow while the court process is expensive and time-consuming for all involved. It is in the interests of both patentees and those who would challenge patents to create a faster, less expensive, route to challenge patents. This must, however, coexist with improving the overall review and approval times for patents at the onset. An expansion of staff and resources in the Patent Office with sufficient expertise in biotechnology will be required to aid in reducing the overall time required for patent approval.

The European Patent Office currently has a patent opposition process under which those opposed to an issued patent have nine months from patent grant to initiate an administrative process to review the patent on any ground. The Canadian government should consider amending the *Patent Act* to include an opposition process similar to that which exists in Europe. This amendment would also bring a measure of certainty to the patent field by providing a mechanism to challenge dubious patents early on with less costs and complication than the existing court-based process. This step would also be a mechanism to reassure the Canadian public that the patent-granting process with regard to genetic patents is itself transparent. In doing so, two goals could be simultaneously achieved: patents ultimately upheld would be more rigorous and therefore ones upon which the patent holders could have greater confidence in, while greater public confidence could be generated in the patent granting process.

9 Revise the Compulsory Licensing System

The Ministerial Conference of the World Trade Organisation in Doha, Qatar in November 2001[72] adopted a declaration dealing with international trade and public health. In that statement, the Ministers (including Canada's Minister of Foreign Affairs and International Trade) stated that nations should be able to take measures "to protect public health and, in particular, to promote access to medicines for all." The Ministers also stated that countries have the right to determine the grounds upon which they will grant compulsory licenses.

In order to prevent the statement from providing a hollow right, the concept of promoting access to medicines for all must include providing access to the diagnostic procedures necessary to determine when and which medicines to provide. The federal government should, therefore, amend the *Patent Act* to specifically allow the potential for compulsory licensing of patents relating to the provision of genetic diagnostic and screening tests should this power be necessary. The compulsory license ought to be granted in return for a reasonable royalty established by the Commissioner of Patents. This royalty should include an amount in respect of the use of the invention, and not profit gained by the patentee through the actual provision of the test. The amendment should not obligate the provinces to first negotiate with patent holders for a licence in respect of these patents. It should, however, require fair payment after determining the relevant factors.

10. Establish a Specialized Court

In Canada, both the federal court and the provincial courts have jurisdiction over patent infringement and determinations of validity. Only the federal court has jurisdiction, however, on appeals from the decisions of the Commissioner of Patents over the refusal to issue a patent.

In contrast, the United States created a single appellate body in the 1980s with jurisdiction over all aspects of patent validity and infringement. This court, the Federal Court of Appeals for the Federal Circuit, has expertise in patent law and technology. This has enabled the court to attempt to shape patent law to address the conflicts which occasionally arise between patentees and the public.

The Federal Court of Canada has less expertise in patent and technology matters. In addition, since the court does not have exclusive jurisdiction over patent matters, it cannot easily shape and interpret patent law to keep pace with scientific progress. While the Supreme Court of Canada has this power, it hears relatively few patent cases. The federal government should, therefore, consider creating a bench of judges with expertise in technology and patent law to adjudicate patent law disputes.

3.7 SUMMARY

Genetic research and technological development is progressing at a speed that outpaces current legislative, policy and regulatory frameworks. While genetic medicine promises incredible benefit to human health, the social, legal, ethical and political issues that accompany these innovations must be addressed. The patenting of genes is a relatively new phenomenon, and gene patents do not fall easily within traditional concepts of intellectual property. There are voices, as we have seen with the Federal Standing Committee on Health, that would ban patents on genes or DNA. Ultimately this approach does not recognize the benefits that can accrue to society by actually promoting innovation. The status quo, however, does not adequately provide sufficient scope of protection against the possible risks that may come with gene patenting.

The nature of genetic research and patents on consequent innovations poses some real challenges to the existing ideological basis of the patent system, and it is important that the rights accompanying gene patents remain consistent with those rights that are attached to more traditional patents. While patents are an important component of genetic research and innovation, the peculiar nature of gene patents requires special treatment in patent law and policy and greater scrutiny by patent examiners.

Both the federal government and the Canadian Intellectual Property Office have a role to play in the development of biotechnological patent law and policy to ensure continued progress and leadership in genetic research and development, while enabling Canadians to enjoy the health benefits promised by this technology.

Viable options are available for Canada to develop an effective and balanced approach to genetic patents that is fair, that respects all international obligations and provides strong intellectual property protection. But in doing so, Canada must have the protections, safeguards and transparency that fully articulates the terms of the contract between inventors and society that a patent codifies. Other jurisdictions have taken steps in this direction, Canada has an opportunity to take important steps of its own. In the longer term, the benefits of doing so will be real both for healthcare and innovation.

This option is certainly more complex, more challenging and more fraught with uncertainty than the approach proposed by the Federal Standing Committee on Health. It is however, perhaps the fairest and most effective way for Canada to balance the risks of gene patenting with the tremendous potential for healthcare flowing from genetic research.

4. Public Perception

Public attitudes and perceptions towards genetic testing will shape the demand for these services. As a highly educated population is being informed about the latest genetic breakthroughs in medicine, healthcare is increasingly becoming a consumer driven industry. Consumers expect and want to take control of their health by avoiding or preventing illness and by taking charge of their own care. It is precisely this trend which will considerably add to the pressure for provinces to adopt and fund the latest genetic technologies.

Genetic testing already has a high level of public acceptance in our society, even recognising the fact that this acceptance is both qualified and not, as yet, fully informed. For example, a PricewaterhouseCoopers survey in Fall/Winter 2000[73] found that over 90% of Canadians supported statements that suggest biotechnology will provide medical benefit.

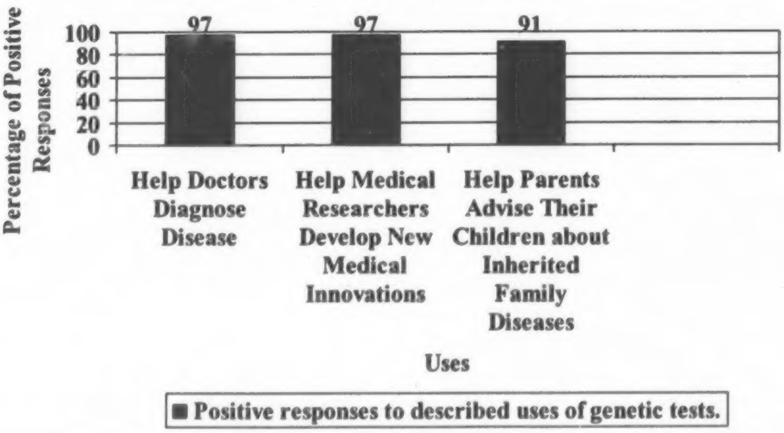
At the same time, though, 90% either strongly or somewhat supported the view that biotechnology could lead to ethical decisions that were troublesome and important to resolve to everyone's satisfaction. In terms of gene patenting, there was no consensus. Half (50%) of the respondents were uncomfortable with patents in biotechnology, whereas 42% supported the view that patent protection for biotechnological innovations was necessary.

However, responses to a 2000 Berger Health Monitor Survey found that Canadians are also very concerned about the use of genetic information.[74] Eight in ten disagree that insurance companies should have the right to require genetic testing as a condition of insurance, and six in ten believe employers should not be told if the employee has a "disease gene" but not the disease.

Focus group testing in Ontario has found great fluidity in public opinions about genetic testing. Many participants appeared to be torn between the benefits they thought genetic testing could bring and the "dark side" uses that could be made of the technology.[75]

POSITIVE PUBLIC PERCEPTION OF USES OF GENETICS TESTS

(From Ipsos Reid Survey of 1000 adult Ontarians, December 2001)

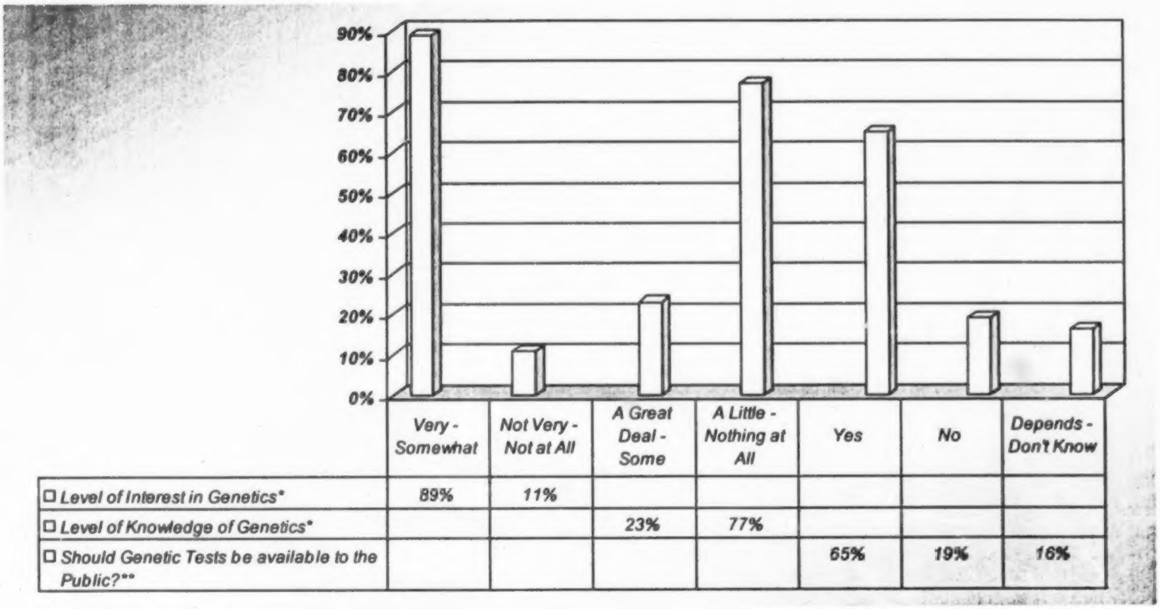


When quantitative polling was conducted, over three-quarters (77%) of Ontarians reported they know very little to nothing at all about the issues surrounding human genetic testing.

Level of Interest/Knowledge of Genetics in Ontario

*Survey of 1000 adult residents across Ontario conducted by Ipsos Reid, December 2001.

**Survey of 1500 adult residents across Ontario conducted by Berger Population Health Monitor with Hay Health Care Consulting Group, January 2002.

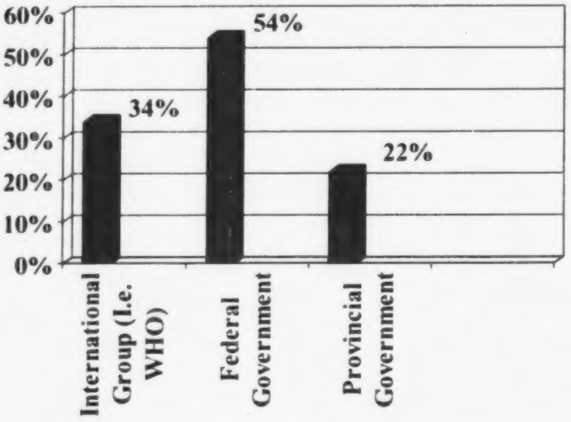


	Very - Somewhat	Not Very - Not at All	A Great Deal - Some	A Little - Nothing at All	Yes	No	Depends - Don't Know
☐ Level of Interest in Genetics*	89%	11%					
☐ Level of Knowledge of Genetics*			23%	77%			
☐ Should Genetic Tests be available to the Public?**					65%	19%	16%

Opinion polling in the United Kingdom and Europe[76] has also shown that public support for gene-based medicine can be mixed. For example, when offered the choice of "magically" curing or preventing disease, there is a generally positive reaction (e.g. in one poll, 75% of respondents were willing to let their children undergo gene therapy for disease). However, when gene therapy was fully explained, the reaction tended to be more negative. The right to privacy of personal genetic information was also a key issue for the public, a fact strongly influenced by a general wariness of third party access to information (particularly employers and insurance companies).

RESPONSIBILITY FOR REGULATING GENETICS TESTS[77]

(From Ipsos Reid Survey of 1000 adult Ontarians, December 2001)



Authors of the U.K. report concluded that although awareness of biotechnology has increased over the past ten years, media reports that emphasize "unnatural" manipulation of genes (e.g. cloning) have generated concerns over its uses. A majority (81%) of Europeans don't think they are adequately informed about biotechnology. There has however been far greater debate about genetics in many parts of Europe than in Canada and we can reasonably anticipate that the numbers of Canadians who might consider themselves "not adequately informed" would be at least as high, if not higher, than Europe.

Although respondents to an Ipsos Reid poll done in Ontario in September 2001, saw a role for the provinces/territories (23%), significantly more (54%) saw the federal government as having responsibility for regulation and 34% saw the need for some international regulations.

In a very recent survey over 60% of Ontarians indicated that if their doctor recommended it, they were very likely or somewhat likely to take a genetic test for an illness or health condition that DOES NOT HAVE A CURE.[78]

4.1 DEMAND FOR TESTING AND SERVICES

No technology can succeed without demand. Three factors will determine the demand for genetic technologies. They are:

a) The public must think of them as desirable and benign, not as unnatural or dangerous;

b) Useful, positive information about the technologies must reach consumers through information sources they trust; and

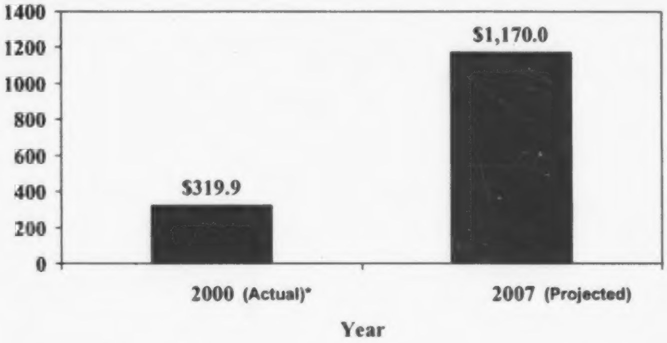
c) The public must exert pressure on health providers and governments to make these technologies available, through the law and legislature if necessary.

As noted previously, there is generally high public acceptance of genetic testing, even recognising the limited knowledge on which this acceptance is based. This interest has already resulted in growing pressure on healthcare systems to provide these services:

> *Numerous studies have suggested that both the general public and patients in at-risk populations already have a high initial interest in accessing genetic testing technologies, and many believe they are entitled to unencumbered access to such services. Benkendorf and colleagues found that 95% of the women in their study thought they should be able to get testing despite a physician's recommendation to the contrary. Similarly, a North American study found that 60% of those surveyed thought that they were "entitled to any [genetic] service they can pay for out of pocket" and 69% thought that "withholding any service was a denial of the patient's rights."* [79]

Despite concerns about the ethics and reliability of genetic testing, this is a rapidly growing area of healthcare. Analysis of the U.S. genetic testing marketing by Frost & Sullivan[80] showed that revenues in 2000 were $319.9 million. Moreover, revenues are projected to jump 273 percent – to $1.17 billion — by 2007.

U.S. GENETIC TESTING MARKET REVENUES (IN MILLIONS)

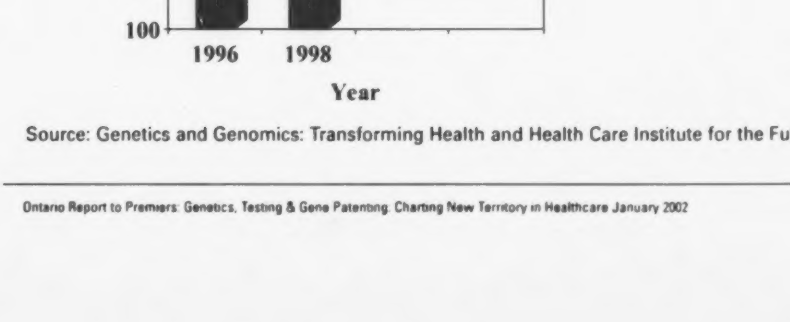


*Source: Frost & Sullivan

4.2 DIRECT TO CONSUMER MARKETING

As consumers take more control of the care they receive and the medical products sought or purchased in that care, direct to consumer advertising will become increasingly important. Already direct to consumer advertising for medical products and pharmaceuticals in the US has increased more than twofold in recent years, from $600 million in 1996 to $1.3 billion in 1998. [81] This increase in spending on marketing cannot help but impact upon Canadian perceptions and demands in the area of genetics.

AMOUNT OF MONEY INVESTED IN DIRECT TO CONSUMER MARKETING FOR MEDICAL PRODUCTS AND PHARMACEUTICALS IN U.S.A.



Source: Genetics and Genomics: Transforming Health and Health Care Institute for the Future, 2000

Although direct to consumer advertising is prohibited in Canada for prescription medications and professional services, it seeps in from US television stations and print media and is freely available on the internet. Direct patient marketing in the area of genetic testing and screening has a serious potential to undermine the beneficial impact of provider education and the provision of counselling, effectively breaking the important link between the test and the overall health system.

As economists from the Centre of Health Economies and Policy Analysis (CHEPA) have rightly noted:

One determinant of behavioural and health responses will be how the benefits and costs of testing, and ultimately of treatments, are communicated to the public, and to practitioners. Unlike most non-genetic screening services, for-profit corporations now hold exclusive patents on many genetic testing technologies. This affects not only the cost of the tests themselves, but also the way that genetic testing is portrayed to providers, and the general public.[82]

In the U.S., genetic services are already being marketed directly to the public. Harvard Pilgrim healthcare, for example, provides a team of physicians and counsellors with expertise in genetics who offer consultation, counselling, testing, support groups, education and referral.[83] In Canada, a private genetic testing clinic based in Saskatchewan had, for about $1,500 been offering customers a profile of their predisposition to diseases such as cancer, heart disease and Alzheimers disease.[84]

It is expected that advertising surrounding genetic technologies will soon become an increasing part of the medical landscape. Direct to consumer advertising may come to play an important role in influencing the adoption and demand for genetic services. Furthermore, if genetic tests are not offered through conventional genetic programs, with appropriate counselling and support, and instead become more and more available as "at-home" kits, significant policy considerations could arise regarding not only the quality of testing available, but the appropriateness of the testing with no formal requirement of patient education or risk management advice.[85]

An example of some of the information contained on websites where individuals are provided the option of directly sending a sample of their blood to a facility for genetic testing.
Sending samples is easy. The kit is easy to use and there is no charge.
It requires only a small amount of blood.

The kit contains the following items:

- ***1 tube to put your blood in***
- ***1 container to hold the tube for shipping***
- ***1 form for you to fill out to request your tests***
- ***1 form for you to sign that gives your consent for testing***
- ***1 form with instructions***
- ***1 form that contains billing and cost information***
- ***1 Express Mail form with pre-printed information***
- ***1 special genetics pencil***

4.3 PAYMENT

Who will pay for the genetic testing the public appears to want? Ipsos-Reid research in Ontario[86] found that 43% of adults stated that the provincial healthcare plan should pay all of the costs for all genetic testing. However, follow-up questions found that consumers also distinguished between different types of tests. The majority thought the provincial healthcare plan should pay *all* of the costs for testing for such disease as cancer (64%), Cystic Fibrosis (60%) and mental illness such as Schizophrenia (54%), as well as any tests recommended by a doctor (63%). Support was much lower for tests for illnesses that effect only a small number of people (only 39% believed that the provincial healthcare plan should cover all of the costs), associated with testing for alcoholism (24%) or tests that individuals themselves want to have done (13%).

4.4 PUBLIC ENGAGEMENT

As genetic testing becomes more common, in whatever form it eventually takes, public engagement and education becomes increasingly important. Effective and specialized communications will be increasingly required to bridge the gap between the differing perspectives, understandings and language routinely used by genetics "experts" (e.g. clinicians and scientists) and the manner in which many in the public perceive both genetics and the nature of such vague concepts as "relative risk."

Below is a chart illustrating the general nature of the divide that sometimes exists between the perceptions of genetics and risk in the public mind and the approach to the science often employed by practitioners.

THE TWO LANGUAGES OF RISK ASSESSMENT [87]

Expert	Public
Approach is scientific	Approach is intuitive
Comfortable with probabilities and percentages	Comfortable with dichotomy (yes/no)
Goal is to establish acceptable risk	Goal is to establish safety
Accepts that knowledge is always changing	Wants a definitive answer (is it or isn't it?)
Considers events in terms of comparative risk	Interested only in current situation (discrete events)
Deals at level of population averages	Concerned with personal consequences
"A death is a death"	"It matters how we die"

If scientific communication with the public is missing or ineffective, a risk information vacuum will develop. This vacuum will not be left empty for long. In the era of day trading on the stock market, many thousands of people are trying to make sense of all types of complex financial data and economic indicators. Consumers who want to be involved with their health as much as their finances, will not hesitate to tackle learning about the human genome. Over time, media reports, the research of educated, active consumers, the perspective of interest groups and intuitively-based fears will combine to fill the information vacuum. A consensus in public opinion may emerge – one that may, or may not, be accurate or informed. At this point, changing public opinion, even in the face of scientific fact, may become difficult or costly – or even impossible.

It is important that the Canadian public be engaged and educated about genetics and genetic testing and their risks and benefits. This engagement is critical if rational decisions are to be made about the uses and financing of these services, and can not be left to chance or interest groups. This function is, in fact, part of the mandate of Genome Canada ("Effectively communicate the results of genomics research to the public, thereby helping Canadians to understand the relative risks and rewards of this type of research").[88] However, the task of education cannot rest with one institution alone if it is to be at all effective. As polling routinely reveals, the gap between the knowledge that Canadians currently have about genetics combined with the obvious desire to access new testing will require a rigorous and organized approach involving health professionals, governments and the biotech sector to be effective.

In the U.K., the Nuffield Trust Genetic Scenario Project[89] has long recognized the need for concerted efforts to raise the level of genetic literacy among the general public. Its recommendations have included:

- Governments should set an open and wide-ranging agenda for discussion about current and future developments in genetics;
- Incorporate education on genetics into school curricula (e.g. elementary and secondary schools, as well as all relevant university disciplines);
- Incorporate the concept of statistical risk into school curricula. The public finds the concept of risk difficult and confusing and clinicians are often poor at explaining it to their patients. For example, numerical explanations often mean very little to the public and decisions are often influenced by how the information is framed (e.g. you have a 10% chance of dying versus you have a 90% chance of living; is a 10% chance of dying within a period of 15 years positioned as high or low?)
- Establish and implement a strategy for the promotion of genetic literacy. This strategy should consider how a concerted campaign might be mounted to raise public understanding of genetics and the issues that surround personal risk.

Creation of effective public education on genetics and risk will require collaboration between many parts of our society (e.g. government, industry, the media, education and healthcare providers, agencies and institutions).

A number of stakeholders should be involved (e.g. representatives from professional organizations, pharmaceutical and biotechnology companies, schools, universities, healthcare providers, the media and voluntary associations representing people affected by genetic diseases). As with any form of public outreach, there is never one "magic bullet" for public education. A number of approaches should be utilized. These might include modifying school curricula, media and public relations, public-awareness building (e.g. advertising) and the creation and distribution of appropriate educational materials.

5. ECONOMIC IMPACTS

Genetic technologies will, in time, come to effect every sector of health, including the public health system, consumers, payers, providers, and drug and technology developers. The changes will follow four broad trends:

- The healthcare workforce and structure will face radical change in terms of required skill sets as new technologies will require the new workforce to have additional knowledge and skills in a complex and rapidly growing field;
- Consumers will become better-educated and more assertive on matters concerning health, effectively demanding access not only to new forms of testing but to the benefits of pharmacogenomics;
- Many genetic technologies while offering promise of longer term savings through better disease management but will in the short-to-medium term likely contribute to the rising costs of healthcare;
- New regulations and policies will need to be enacted to govern the use and development of genetic technologies.

According to the Canadian Institute for Health Information, healthcare spending in Canada broke the $100 billion mark in 2001. Over the last four years, healthcare spending has grown at annual rates of over 6.5%, a substantial increase over the early to mid-1990s. This growth largely reflects increased spending by governments and in 2000-2001 the percentage of private funding for healthcare actually declined slightly as a proportion of the total.[90]

5.1 PARADIGM SHIFT

In a publicly funded system, any use of resources for genetic testing may impact on the availability of resources for other health needs. This is particularly true as most new technologies tend, at least initially, not to replace but rather to complement other existing techniques. One of the latest breakthroughs in diagnostic imaging, the Positron Emission Tomography (PET) scanner, tends to be used not wholly to replace a conventional MRI or CT scan, but to perform a greater level of investigation on an individual who has already been screened using other techniques. We can anticipate that a number of genetic tests (especially certain predictive tests) will not wholly replace existing tests but will co-exist with them.

As new genetic tests come to market and practitioners and consumers demand access to them, the capacity for provinces to undertake effective, co-ordinated and comprehensive health economic analysis on the new tests will be critical. Without such objective and critical appraisal, it is highly likely that hype and lobbying regarding access to new "breakthrough" tests and interventions will shape coverage of tests.

About half of the increase in the cost of healthcare is generally thought to be attributable to the use and cost of new technologies. As the technology develops (e.g. as the DNA chip becomes cost effective and increasingly available) it is expected that the cost of genetic testing will fall. But the impact of genetics and biotechnology on the heath care system will be felt in many different ways, arguably, the least of which may be the cost of the test.

Economists from the Centre for Health Economic Policy Analysis (CHEPA) make the following points:

> **"Where preventative therapies currently exist, genetic testing services may also be promoted by those selling these goods and services that could be seen as complementary to the genetic test. This has occurred in the case of non-genetic screening programs - e.g., bone-densitometry, serum lipid testing - where specific companies selling drugs to manage those risk factors have financial interest in promoting the screening programs themselves. Current models of pharmacological disease management may evolve along with genetic testing, offering products and services to the "market segment" created by those determined to be at greater than standard risk of given illnesses. In many cases, the cost of complementary treatments will exceed (possibly by far) the cost of the genetic testing itself."[91]**

Proponents have argued that since the certain genetic tests are predictive, better prevention could be practiced and healthcare costs, as a result, reduced.[92] For certain tests, this may be the case, however, it is a leap of logic to assume simply because a predisposition to a certain disease or condition is identified that lifestyle changes will naturally follow. This is far from the case with conventional diagnostics. One recent Health Economic Study put it in these terms:

> **"The evaluation of preventative responses to genetic testing services (including pharmacological disease management responses) is critical for determining the overall cost of genetic testing service. This task will not be easy. Clinical benefits from preventative products and services consumed upon the identification of genetic susceptibility to many illnesses will not be observable for many years in some cases decades. As the time line involved becomes longer, the savings or health improvements required to justify ongoing costs of prevention must increase...**
> **The costs of treating susceptible populations with such therapies will, nevertheless, add up over time as we wait for evidence of long-term efficacy."[93]**

Moreover, the most appropriate response to a certain test showing an elevated genetic risk of a certain disease or condition may well, in addition to certain lifestyle changes, also take the form of pharmaceutical intervention. In this case, the costs to the system over the long term increase and potentially increase significantly. This is especially true when we consider that predictive tests detect risk in many cases in the asymptomatic individual, thereby potentially expanding the window of medical intervention significantly. Understanding the full implications for the costs of conventional treatments in this paradigm will become increasingly important for health system planners to understand. As scientists from CHEPA have noted:

> **"The importance of the treatment or preventative therapy that follows genetic testing services highlights a consideration regarding the funding of genetic testing services themselves. The cost of genetic testing itself may be outweighed by the costs related to services induced by the test results. Consequently, whether or not a test is provided publicly, much of the cost associated with goods and services complementary to the test will be born by the public system".[94]**

Certain forms of genetic testing may also actually increase the numbers and types of conditions for which medical intervention is undertaken. Conditions or diseases that were previously untreatable and that could rarely be identified, may increasingly, as our capacity to both detect and predict risk of disease improves, actually come within the scope of being manageable conditions for which treatment is available. Whether and to what end such a macro-shift in healthcare takes place we can only speculate. It is, however, certainly within the boundaries of the possible.

In addition, some have actually gone as far as to state that developments in biotechnology may help to increase our life span (some researchers have even estimated that the average North American life span may extend to 95 years by 2050). A population in which more people live longer will naturally escalate the demand for healthcare services, which tend, as has been well documented, to be more heavily utilized as the population ages.

Reshaping health human resource capacity to make optimal use of new genetic breakthroughs will carry significant costs for our healthcare system. These costs will be felt in a range of areas:

- Hospitals, will need to develop new competencies in genetic technologies or form alliances with centres that do. Developing these competencies will potentially require significant investment in both equipment and trained personnel. At the same time, these changes may also push hospitals to rethink their delivery systems, staffing and technological capabilities.

- Training will become a major priority across a range of health specialties. More genetic specialists will be required and adequate recruitment and retention mechanisms will need to be put in place by jurisdictions offering genetic testing. This may become more pronounced as demand from the private sector and other jurisdictions attract a healthcare resource in short supply (geneticists). This training will also be important for family physicians, nurses and other healthcare providers. As well, health systems and medical centres will have to adjust their own internal educational and training programs and even reconfigure staffing to meet the changing needs of gene-based medicine.

- Genetic counselling services and specialized laboratory services will need to be expanded, not only to address the current demand for testing, but to adequately meet future demand.

- New mechanisms and in some cases new structures will likely be called for to oversee the quality of laboratory testing, whether privately or publicly delivered.

5.2 HEALTH ECONOMIC ANALYSIS: CASE STUDIES

In a report prepared by the Centre for Health Economics and Policy Analysis (CHEPA), McMaster University,[95] it is noted that the specific economic impact of a particular new genetic test is not easily determined in advance and ultimately depends upon a complex interaction of a number of factors, such as:

- the test's sensitivity (the probability that a test will be positive in a person with the condition) and specificity (the probability that a test will be negative in someone who does not have the condition);
- the quality (accuracy) of the testing process;
- how the test is used in the healthcare system;
- the scope of screening programs based on the test;
- compared to current clinical practice, the test changes costs for testing, disease surveillance, prevention and treatment (i.e. what each person does based on the information provided by the genetic test).

The following table summarizes the potential impact of genetic tests on types of healthcare costs, depending upon a number of potential factors. For example, the table shows that if there were currently no diagnostic test for a condition, the introduction of a genetic test would increase costs. If a genetic test replaces a current diagnostic test, costs could either increase or decrease, depending upon the relative costs of the two tests. However, if a genetic test was to be performed in addition to the current diagnostic test, healthcare costs would definitely increase.

POTENTIAL IMPACT OF GENETIC TESTING ON HEALTH CARE COSTS (CHEPA, 2001)

Population Who Receives the Test		Types of Costs to Health Care System			
Disease Status	Post-Test Status	Costs Associated with Case- finding when current practice is...	Costs Associated with Surveillance when current practice is...	Costs Associated with Prevention when current practice is...	Costs Associated with Treatment when current practice is...
		a. no current test b. genetic test replaces current test c. genetic test in addition to current test	d. no surveillance for anyone e. surveillance for high risk (HR) individuals f. surveillance for general population	g. no preventive treatment h. preventive treatment for high risk (HR) individuals i. preventive treatment for general population	j. intervention specific to condition
Compared to the current world without a genetic test, the introduction of a genetic test will have the following effects on health care costs for each identified type of individual for each alternative type of current practice pattern: Those with the disease (or who will get it eventually) True Positive increase					
Those with the disease (or who will get it eventually)	True Positive	a. **increase** b. **increase** or decrease depending on relative costs of tests c. **increase**	d. no change e. previous HR: no change previous LR: **increase** f. no change or **increase** if surveillance intensified	g. no change h. previous HR: no change previous LR: **increase** i. no change or **increase** if treatment intensified	j. reduced if prevention effective or early detection or early detection less costly to treat
	False Negative	a. **increase** b. **increase** or decrease depending on relative costs of tests c. **increase**	d. no change e. previous HR: decrease previous LR: no change f. decrease	g. no change h. previous HR: decrease previous LR: no change i. decrease	j. no change or **increased** if failure to detect early increases costs
Those without the disease (or who will never get it)	False Positive	a. **increase** b. **increase** or decrease depending on relative costs of tests c. **increase**	d. no change e. previous HR: no change previous LR: **increase** f. no change or **increase** if surveillance intensified	g. no change h. previous HR: no change previous LR: **increase** i. no change or **increase** if treatment intensified	j. no change
	True Negative	a. **increase** b. increase or decrease depending on relative costs of tests c. **increase**	d. no change e. previous HR: decrease previous LR: no change f. decrease	g. no change h. previous HR: decrease previous LR: no change i. decrease	j. no change

Using a decision analytic model, CHEPA looked at the effects of genetic testing in three cases: Familial Adenomatous Polyposis (a rare hereditary syndrome which can lead to colorectal cancer (used original costing study), Hereditary Nonpolyposis Colorectal Cancer and hereditary hemachromatosis (used existing literature for costing study). In this section, results of these studies will be summarized briefly (Executive Summary, Bigger Picture and, Conclusion of the CHEPA report is available in Appendix 3 The entire report will be available on the Ontario Government website).

Familial Adenomatous Polyposis (FAP)

As explained, FAP is a rare hereditary syndrome caused by mutations in a single tumour-suppressing gene. Individuals with FAP develop hundreds of polyps in the colon at an early age and are nearly certain to develop colorectal cancer by age 50 years. Because it is rare, population screening is not recommended. First-degree relatives of individuals with FAP have a 50% chance of inheriting the disease and should be tested by flexible signmoidoscopy from age 10 onwards, repeated every 2 years until age 40 and every 3 to 5 years thereafter until age 60. In the "genetic testing" scenario, a genetic test is conducted on the proband (the person with FAP) and, if positive, on first-degree relatives. Colonscopic surveillance is then required for the proband and only those relatives for whom genetic test results are positive or inconclusive.

After accounting for the number of first-degree family members, the age distribution of the relatives, the age-dependent clinical screening profiles, and discounting of future costs (at a rate of 5% per year), the expected costs of the conventional surveillance strategy was estimated to be $9,607. By comparison, the expected costs of the genetic testing strategy were estimated to be $8,238. Thus, the net savings per FAP family was about $1,369. Genetic testing continued to be cost-effective even if the cost or sensitivity of the test changed. However, results were sensitive to the cost estimates for the clinical surveillance and assumed family size. For example, if the cost of colonscopic surveillance drops below $2000, the genetic testing model was no longer less expensive than the conventional surveillance.

Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

HNPCC is a rare Mendelian disorder that is associated with an 80 to 90% risk of cancer (a 80% lifetime risk of colorectal cancer, a 43 to 60% risk of endometrial cancer, a 13 to 19% risk of gastric cancer, a 9 to 12% risk of ovarian cancer, and elevated risks of several other forms of cancer). Unlike FAP, HNPCC is associated with several genes, which makes testing less accurate.

Analysis of existing economic studies of HNPCC testing indicates that although there may be net benefits (savings) from genetic testing targeted at families with a history of the disease, population screening is unlikely to be cost effective. Population screening for HNPCC could be beneficial only if surveillance and preventative treatments are 100 percent effective at preventing colorectal cancer, the genetic test had 100 percent sensitivity and specificity, tests were supplied at cost, and the prevalence of HNPCC was in the order of 1 in 100 to 500 individuals.

Hereditary Hemochromatosis (HH)

About one in ten people of northern European descent carry a recessive gene for hereditary hemochromatosis (high levels of iron in bodily tissues, especially the liver, heart and joints). If left untreated, iron saturation can result in liver disease, diabetes or heart disease. If the disease is detected before serious organ damage has begun, it can be safely and effectively treated (the main treatment being regularly bloodletting or phlebotomy).

The high prevalence of hereditary hemochromatosis, the non-specific nature of its early signs and symptoms, and the low treatment costs make this disease an excellent candidate for population screening among people of northern European descent. Previous research suggests that clinical screening followed by genetic testing may be more cost-effective than genetic screening followed by surveillance. Where possible, focused genetic testing (i.e. genetic testing for family members of individuals with confirmed cases) is more cost-effective than broad screening.

5.2.1 WHAT DOES THIS MEAN?

In looking at patterns of test characteristics, genetic testing programs, and cost situations and how they interact to determine the impact of the introduction of a test on healthcare costs, various factors come into play. "Dream" genetic tests will exist, those that will result in lower costs for the healthcare system with potentially positive health impacts and 'nightmare predictive genetic tests' that will result in significant costs for very limited or non-existent health benefits.

However, as economists from CHEPA note: "Because their potential application is so broad, predictive genetic risk-factor tests have the potential to change the healthcare seeking (providing) behaviours of large numbers of individuals (providers), risk factor tests have the potential to generate the greatest range of cost impacts.

Risk factor tests brings to mind Longfellow's nursery rhyme: "When she was good, she was very, very good. But when she was bad, she was horrid."

For example, a risk-factor test for coronary artery disease could result in large numbers of people taking cholesterol lowering drugs for decades. Even if reasonably effective, such tests could impose large costs in the near future to avoid treatment costs (and provide health benefits) long into the future.

This potential for large cost impacts implies that risk factor tests call for particular scrutiny and particular care in designing the programs through which they will be delivered. Even good tests, when misapplied, can generate large cost impact. **These risk factor tests may also pose some of the greatest challenges, as they are the type of**

test most likely to be marketed directly to consumers and most likely to be applied in a much broader range of situations than those initially approved. There is a direct analogy to the experience with many drugs, which gain approval for use in a narrow set of circumstances according to well-defined criteria but which, once on the market, are prescribed for a wide range of situations not initially intended.

In contrast, because they are generally associated with rare genetic disorders, the narrowest range of cost impacts arise with presymptomatic, single-gene tests. Even when such tests generate large savings in each individual tested, the total cost savings are small. Similarly, even when such a test increases cost, the total cost increase is small. (See case study FAP above.)

Finally, in between these two extremes are the susceptibility predictive tests. Like presymptomatic tests, they often have high predictive power, but like risk factor tests, their potential scope of application is sometimes quite broad. One of the most widely discussed tests of this type is BRAC1 and BRAC2 which test for mutations to the genes associated with breast ansd ovarian cancer. (Other such tests are HNPCC, a particular form of colorectal cancer, and a predictive genetic test for HH in case studies above").[96]

5.2.2 BUILDING OUR CAPACITY TO ANALYSE

The work undertaken by CHEPA to analyse the impact and the decision scenarios which would be required to determine the immediate impact of a single new test being funded, illustrate well the sheer complexity of the types of determinations that will need to be made at the level of the individual test.

What the analysis to date is unable to do, and this is due in part to the relative lack of macro-level studies on the system impact of new genetic technologies, is to tell us what the cumulative medium to long-term impact on overall health system spending will be of the incorporation of a range of new tests and interventions over a relatively short period of time. This cumulative effect, above and beyond the incremental cost of a single new test, combined with the possible changes to the treatment window brought about by more use of predictive testing will introduce perhaps more radical economic impacts than the cost of testing per se and have potentially the greatest impact on long term sustainability of the healthcare system. It is precisely these system level costs, human resources, training, counselling and capital that stand to impact the health system most.

There is, therefore, an urgent need for governments to strengthen their collective capacity to assess the potential medium-term impact of genetic technologies. Such an assessment would need to examine not only tests that are coming down the line, but critically, the system level human resource needs and implications and the corresponding impact on healthcare delivery. As significantly, the potential for predictive testing to change individual behaviour thereby effecting utilisation of conventional healthcare resources needs also further examination. With the possibility for medicine to be "redefined in our lifetimes," and with the cost additive in the near term, provincial, territorial and federal governments will be required to make significant financing choices.

6. CAPACITY TO DELIVER: HUMAN RESOURCES

The delivery of genetic testing in the future will be challenging. With the development of new modes of testing and the possible impact of patents influencing the costs, locations and forms that testing will take, no one can say for certain how tests will be administered, by whom they will be administered, or how results will be interpreted and ultimately delivered to the consumer.

On the human resource side however, there are two main issues. Firstly, almost without question, there will be a growing need across Canada for the training and recruitment of more genetic specialists to meet future needs. This relative shortage is already evident now in most jurisdictions that offer testing and will only grow more pressing as new tests and interventions are introduced. Secondly, genetics is a growing field and one that very quickly will need to move from primarily a domain of labs and specialists into the day-to-day practice of primary care physicians, nurses and other healthcare professionals. The education of our general health professional workforce in genetics to prepare for this shift is, therefore, something that all jurisdictions will need to view as a priority.

6.1 GENETICISTS

Currently there are estimated to be about 1,800 genetic counsellors (one per 150,000 people) practicing in the US and only 22 training programs.[97] In Canada, the situation is similar. The following table summarizes the number of clinical geneticists and genetic counsellors in several Canadian provinces.

Province	Population*	Geneticists**	Number of Geneticists per Person	Genetic Counselors***	Number of Genetic Counselors per Person
Ontario	11, 847, 000.00	28[i]	1 per 423,107.00	100	1 per 118, 470.00
Quebec	7, 410, 000.00	13[ii]	1 per 570, 000.00	19	1 per 390, 000.00
British Columbia	4, 095, 000.00	7[iii]	1 per 585, 000.00	18	1 per 227, 500.00
Alberta	3, 064, 000.00	9[iv]	1 per 340, 444.00	TBD	TBD
Manitoba	1, 150, 000.00	5 (one works part time)[v]	1 per 230, 000.00	6 (but 1.5 positions are currently vacant)	1 per 191, 667.00
Saskatchewan	1, 015, 000.00	1[vi]	1 per 1, 015, 000.00	2	1 per 507, 500.00

i. This is the number of geneticists in Ontario's genetics centers and includes 22 Ph.D. geneticists. The Royal College of Physicians and Surgeons of Canada states that there are 13 certified medical geneticists in Ontario (2000).
ii. Number from Association des Médecins Généticiens as of June 2001.
iii. From Medical Directory College of Physicians and Surgeons British Columbia 2000/2001.
iv. This number reflects the number of physicians who specialize in medical genetics, from The College of Physicians and Surgeons Alberta.
v. From Health Services Utilization and Research Commission report "Preparing for Future Possibilities in Genetic Testing" October 2001: page 17.
vi. Ibid.

* These populations for 2001 have been rounded to the nearest thousand. Source: Statistics Canada http://www.statcan.ca/english/Pgdb/People/Population/demo02.htm.

** The number of geneticists listed are approximate numbers to the closest estimations available.

*** Approximate numbers given through personal communications with other Ministries of Health or found in reports that give approximate estimations.

In 1991, the Science Council of Canada released a survey of ten genetic centres in Canada conducted in 1986/87.[98] Even at that stage, *eight of the ten centres were unable to meet the demand for their services*. Since that period the number of genetic tests offered has increased at a rate far greater than the corresponding increase in specialized expertise. Over the next ten years, as genetic testing becomes more common, there will be a critical need for genetic counsellors to help consumers interpret the results.

Given the anticipated need for genetic counsellors, does our educational system currently have the capacity to meet this demand? Presently, only three Canadian universities have genetic programs. McGill University accepts two students a year in its genetics counselling program. The University of British Columbia and the University of Toronto offer two-year programs leading to a Master of Science degree in genetic counselling. It is anticipated that all graduates of these programs will meet the minimum standard required to sit the certification examinations for the Canadian Association of Genetic Counsellors and/or the American Board of Genetic Counselling.

As well as genetic counsellors, there is a growing need for medical geneticists. The World Health Organization places the number of geneticists to adequately serve a population at one per 200,000 people. In the United Kingdom, a standard has been set at one per 500,000 people.[99]

Addressing the needs for medical geneticists will be difficult given the current lack of training opportunities. There are currently only two medical schools in Ontario that offer five-year residency program in Medical Genetics (University of Ottawa and the University of Toronto). Training in medical genetics is a specialty program that is accredited by the Royal College of Physicians and Surgeons of Canada. In 2000 and 2001, one position in genetics was filled each year. For the 2002 academic year, a total of two positions in medical genetics will be offered.

It is perhaps worth noting that other jurisdictions have been faster to recognise and respond to what will be a future pressure. In the UK, the National Health Services has developed ambitious plans to expand genetic services[100]. A budget of more than 30 million pounds ($75m CDN) has been allocated in order to double the number of genetic specialist consultations over the next five years. In addition, a 10 million pound ($23m CDN) Genetic Knowledge Challenge Fund has also been established to create four genetic "knowledge parks" to bring together scientific and medical expertise.

6.2 GENETIC EDUCATION FOR OTHER HEALTH PROFESSIONALS

A survey of participants at a National Institutes of Health meeting ("Incorporating Genetics into Medicine and Nursing Education and Practice", April 1995) found that 76% of respondents thought that the lack of genetic knowledge on the part of healthcare providers was a major barrier to integrating genetics into primary healthcare.[101] This finding supports the recommendation of the Nuffield Trust Genetics Scenario Project calling for action to promote the systematic incorporation of information on genetics and the concept of statistical risk into the training and education of all health professionals.[102]

In the absence of an adequate supply of geneticists, primary care physicians, pediatricians, obstetricians, and other clinicians will be increasingly called upon to counsel and advise their patients on issues surrounding genetic testing. However, many physicians will almost certainly find it difficult to keep up with all of the new information surrounding genetics and many are not currently well prepared to do so.

Although all physicians receive a basic training in genetic susceptibilities, they may not be prepared to counsel their patients, particularly in the case of presymptomatic and prenatal testing which often pose complex psychological and ethical problems. Physicians will therefore need to acquire more knowledge about the benefits, costs, limits and the legal and ethical ramifications of these tests. Who should take responsibility for this educational effort? How will physicians and patients be supported in making these decisions?

Physicians are not the only health professionals who will be affected by the growth of gene-based healthcare. In the future, nurses will, in all likelihood, find themselves in the position of communicating risk information to, and interpreting genetic tests and therapies for, patients. Nurses will need to become familiar with the new terminology, concepts, technology and treatment options of gene-based medicine.[103]

Pharmacy programs may also need to expand their current programs in genetics and genomics in anticipation of the widespread application of pharmacogenetics to drug related activities. Pharmacists will need to be informed and educated about genetics in order to understand and effectively use the new generation of personalized medications and the role that genotyping may come to play in the routine prescriptions of basic medications. **With genotyping and the development of drug risk profiles anticipated by some in industry within the next two to six years, there is little time to fully prepare for these changes.**

Because gene technology is more complex than many of our existing clinical interventions, without greater provider education, one side effect will likely be that the relationship between vendor representatives (sales representatives) and physicians will undoubtedly change. An imbalance of information could easily emerge, which may make physicians more dependent upon the expertise of sales representatives. As a result, the educational role of the vendor may increase and become more influential in driving uptake of these new genetic technologies by providers. This imbalance is potentially detrimental to both evidence-based care and, if pronounced, to medium and long-term resource allocation.

7. Oversight and Regulation

In some respects, genetic information has much in common with other types of health information. However, there are a number of ways in which genetic information is different. For example, new technologies such as the DNA chip will greatly increase the speed of testing and the volume of information that can result from even one sample. This technology will make possible the rapid creation of large, comprehensive computerized databases of genetic information, the uses of which could be multiple.

All of these factors raise new and unique ethical, legal and regulatory issues that may require innovative regulatory measures.[104] Appropriate and timely research (i.e. health technology assessments) will also be needed to help guide the development of adequate and effective regulatory mechanisms and to assist jurisdictions in determining the sorts of tests and interventions they should consider funding. The realm of ethics will begin to move more centrally into the day to-day debates in healthcare and policy.

We can perhaps learn from steps that have already been taken in other jurisdictions in order to be able to begin to craft the basis of a workable cross-jurisdictional framework on genetics.

The need for regulation already exists, but will become more acute once genetic testing becomes more widely available, kit-based and fully automated. Appropriate policies regarding the approval and monitoring of home diagnostics and direct to consumer marketing of tests will be needed. As part of this process, governments will also need to determine in what circumstances to make provisions to ensure that consumers receive the appropriate package of services (e.g. counselling) needed for genetic testing. In some cases this may require prohibiting or restricting access to certain forms of tests or placing conditions upon their approval.

Much work remains to be done in Canada to more effectively put in place the mechanisms that will be required as genetic testing and gene-based medicine expands. In contrast, many countries have already enacted legislation and/or guidelines. For example, in France the National Consultative Ethics Committee for the Life and Health Sciences has released opinions and guidelines related to genetics since the early 1980s, on predictive genetic testing in 1996 and on related ethical issues in 1998.[105]

These latter dispositions were subsequently adopted by the French Parliament in 1994 within the framework of the "Bioethic Laws." In 1996 a report, "Genetics and Medicine: From Prediction to Prevention" was published which outlines the ethical principles that must be respected in testing for genetic disorders. For more examples of national legislation, refer to Appendix 1.

Many international organizations and organizations in other jurisdictions have also developed frameworks or guidelines specific to governing the provision of genetic services. This information, together with extensive work undertaken by some jurisdictions in Canada, (e.g. Ontario, Saskatchewan) can provide valuable insights for all provinces and territories as attempts are made to pull together a coherent interjurisdictional framework.

Some examples that can be drawn upon include the work examining regulatory frameworks in various aspects of genetics undertaken by the World Health Organization, World Medical Association, European Commission, Council of Europe, Austria, Belgium, Denmark, Estonia, Finland, France, Germany, Italy, Lithuania, Norway, Portugal, Russia, Sweden, Switzerland, Netherlands, United Kingdom and the United States. Refer to Appendix 1 for more comprehensive, annotated listings of what has occurred in other countries.

In addition, for healthcare professionals, many professional associations have developed detailed positions and policies about genetic testing and gene patenting (e.g. World Medical Association, American Medical Association, American College of Medical Genetics, Canadian College of Medical Geneticists, British Medical Association, Human Genetics Society of Australia, etc.). Please refer to Appendix 2 for a list of the relevant associations and summaries of their positions.

One of the jurisdictions that has perhaps taken the most active role in regulating and establishing a framework for the role of genetics in society is the United Kingdom.

7.1 HUMAN GENETICS COMMISSION (U.K.)

In the U.K., a Human Genetics Commission was created in 1999 to address issues concerning the use of genetic information.[106] The Commission took over the role of three previous advisory committees: the Human Genetic Advisory Committee, the Advisory Committee on Genetic Testing and the Advisory Group on Scientific Advances in Genetics. The Human Genetics Commission is one of three strategic scientific advisory bodies that have a policy evaluation, as well as an advisory role to the U.K. government. The other two bodies are the Food Standards Agency and the Agriculture and Environment Biotechnology Commission.

To date, the Commission has proposed policies on genetic testing in employment[107] (see section 7.3) and has helped to negotiate a voluntary five-year moratorium on the use of genetic testing by the Association of British Insurers.[108, 109] A key role of the Human Genetics Commission is to promote debate, to listen to and gather public and other stakeholders' views, to consider these thoroughly and to provide expert advice to the government. The Commission makes possible a national effort in addressing some of the critical issues raised by genetic testing and gene patenting.

The Human Genetics Commission has also stated that it has a number of priorities for further consideration, including:

- to review the use of family history information as part of the wider review of personal genetic information;
- to identify means of ensuring access to affordable insurance for those affected by a genetic condition;
- to promote openness about underwriting decisions involving genetic factors and the information given to consumers;
- to study wider regulatory and arbitration systems for genetic information and insurance; and
- to consider the role of insurance and the use of genetic information with the British social and healthcare system.

7.2 INSURANCE

As noted earlier, one of the key activities that has been undertaken by the Genetics Commission was the negotiation of a moratorium on the use of certain genetic information by the U.K. insurance industry. The moratorium covers the use of genetic test results when selling life insurance coverage up to 500,000 pounds (approx. $1.35m) and other coverage up to 300,000 pounds (approx. $700,000)

The Association of British Insurers said that the ban is binding on all its members, which make up 97% of the industry. The ban was motivated by concerns about testing accuracy. Huntington's Disease is the exception because the test has proven accurate. Currently accuracy testing for breast/ovarian cancer and Alzheimer's disease is being conducted by the Genetics and Insurance Commission.

In the U.S., the federal *Americans with Disabilities Act* may cover an individual with positive test results for genetic conditions and prohibits employment discrimination on that basis. However, the employees must prove that their employers have discriminated against them because of a perceived disability based on genetic information. As well, the *Health Insurance Portability and Accountability Act (HIPAA)* of 1996 prohibits the use of genetic information by insurers to limit eligibility for group health insurance plans and specifies that genetic predisposition will not be considered a pre-existing condition. However, the HIPAA only applies to employer-based and commercially-issued group health insurance. There is no similar law applying to private individuals seeking health insurance in the individual market. Also, the legislation does not prevent insurers from requesting or requiring genetic testing or from obtaining the results of genetic tests carried out and it provides little protection for individuals outside group plans. Two other federal acts have been drafted but at this point have not been voted upon: the 1997 *Genetic Information and Non-discrimination in Health Insurance Act* and the 1997 *Genetic Confidentiality and Non-discrimination Act*.

Historically in the U.S., insurance has been regulated by the individual states. Thirty-five states have currently enacted legislation regarding genetic discrimination in insurance. In addition, over 100 bills were introduced in the 1999 state legislative sessions regarding genetic discrimination by insurers and/or employers. Almost all the enacted legislation applies only to health insurance, however, a few states have adopted a more inclusive approach. For instance, legislation in South Carolina prohibits all insurers from discriminating on the basis of genetic information, by terminating, restricting, limiting or otherwise applying conditions to coverage of any individual; canceling or refusing to renew coverage; excluding from coverage; imposing a waiting period; or establishing a differential in premium rates.

The South Carolina legislation also explicitly prohibits the disclosure of genetic information to a third party without written informed consent, and the performance of a genetic test without informed consent. It also prohibits insurers from requiring a person to consent to disclosure of genetic information as a condition of obtaining insurance. In this way, this legislation attempts to fill gaps left by HIPAA.

Maine has also enacted comprehensive legislation. In Maine, insurers are prohibited from discriminating on the basis of genetic information in the issuance, withholding, extension, renewal, fixing of premiums or any other terms in the issuance or acceptance of insurance. The events that are protected during these activities are the refusal to submit to a genetic test or make available the results of a genetic test or on the basis that the individual or eligible dependent received a genetic test or genetic counselling.

Maine legislation also prohibits life, disability and long-term care insurers from making or permitting any unfair discrimination against an individual in the application of genetic information or the results of a genetic test in the issuance, withholding, extension or renewal of any insurance policy for: life; credit life; disability; long-term care; accidental injury; specified disease; hospital indemnity; or credit-accident insurance. "Unfair discrimination" in the legislation includes but is not limited to the application of the results of a genetic test in a manner that is not reasonably related to anticipated claims experience.

The more typical, less inclusive approach of state legislators is Colorado, which only prohibits utilization of information derived from genetic testing from being used to deny access to healthcare insurance. In Connecticut, legislation only applies to health insurers, but prohibits insurers from refusing to insure, refusing to continue to insure, or limiting the amount, extent or kind of coverage available to an individual because of genetic information. It also prohibits health insurers from charging an individual a higher premium for the same coverage because of genetic information.

One important fact to note is that few legislative approaches include genetic information from any and all sources. Many states permit insurers to consider family history of disease and observed clinical signs and symptoms of medical conditions.

In Canada, while the federal government and a number of jurisdictions have privacy regimes in place, few have anticipated the challenges of specifically regulating genetic information.

7.3 EMPLOYMENT

In the U.S., more progress in legislation has been achieved at the state level. Former U.S. President Clinton signed an Executive Order in February 2000 that prohibits genetic discrimination in the federal workplace. Some argue that this executive order should extend to all workplaces in the U.S. Over 23 states have enacted legislation regarding the use of genetic information in employment. Some of the older legislation is limited in its scope, (e.g. offering protection only against certain disorders such as Sickle Cell Anaemia). More recent legislation, however, tends to provide more comprehensive protection. In North Carolina, for instance, employers are prohibited from refusing to employ any person, or from discharging any person from employment, on account of a request for genetic testing or counselling services, or on the basis of genetic information obtained concerning the person or a member of the family. In New York, legislation prohibits employers or licensing agencies from refusing to hire or employ or to bar or discharge from employment on the basis of genetic predispositions or carrier status. Employment agencies are also prohibited from considering genetic predisposition or carrier status when acting upon applications for its services or in referring an applicant to an employer. Other prohibitions relate to: (a) advertising a limitation based on predisposition or carrier status; (b) soliciting, requiring, purchasing, acquiring or contracting to obtain genetic test results or administering or causing to be administered a genetic test in any manner; and (c) requiring genetic testing as a condition of employment unless such test is shown to be directly related to the occupational environment.

The issue of genetic testing in the workplace and the use of genetic information by employers has also spurred activity in the U.K. where a set of proposed principles were previously released by the Human Genetics Advisory Committee to inform discussion in the U.K.

7.3.1 POLICY PRINCIPLES ON GENETIC TESTING IN EMPLOYMENT AS ORIGINALLY PROPOSED BY THE HUMAN GENETICS ADVISORY COMMITTEE (U.K.)

i) an individual should not be required to take a genetic test for employment;

ii) an individual's "right not to know" their genetic constitution should be upheld;

iii) an individual should not be required to disclose the results of a previous genetic test unless there is clear evidence that the information it provides is needed to assess either current ability to perform a job safely or susceptibility to harm from doing a certain job;

iv) employers should offer a genetic test (where available) if it is known that a specific working environment or practice, while meeting health and safety requirements, might pose specific risks to individuals with particular genetic variations;

v) for certain jobs where issues of public safety arise, an employer should be able to refuse to employ a person who refuses to take a relevant genetic test;

vi) any genetic test for employment purposes must be subject to assured levels of accuracy and reliability, reflect best practices... and any use of genetic testing should be evidence-based and consensual;

vii) results of any test undertaken should always be communicated to the person tested and professional advice should be available. Information about and resulting from the taking of any test should be treated in accordance with Data Protection principles. Furthermore, test results should be carefully interpreted, taking account of how they might be affected by working conditions; and if multiple genetic tests were to be performed simultaneously, then each test should meet the standards set out in (ii), (iii) and (iv).

7.4 STRIKING THE APPROPRIATE BALANCE

The Nuffield Trust Genetics Scenario[110] (UK) emphasized, as indeed many have noted, that governmental regulation in the area of genetics and genetic information is needed to protect the interests of the public. At the same time, the Trust has stated that regulation itself should not be crafted in such a way as to put a "stranglehold" upon industry or prevent further research and development. In other words, regulation must strike an appropriate balance between controlling and enabling developments in genetics. Regulations should build upon fundamental principles shared by stakeholders throughout society (e.g. respect for the privacy of individuals).

Canada has a good basis of legislative and regulatory frameworks upon which to build to begin to match the steps taken in other western nations to create the appropriate structures required to address the many issues created by genetic testing.

To maximise this opportunity, will however, demand that governments develop mechanisms, either formal or informal, to ensure that issues of national and international magnitude are not dealt with in an isolated or fragmented manner. This will likely require that jurisdictions begin to work to outline common principles and goals with regard to oversight and regulation of genetic technologies and information. A key part of facilitating this work will be to ensure that appropriate shared forums are put in place, perhaps even a single institution or commission to draw together our resources.

7.5. HEALTH TECHNOLOGY ASSESSMENT

Central to any efforts to regulate gene-based medicine will be health technology assessment studies. The Canadian Co-ordinating Office for Health Technology Assessment[111] defines health technology assessment as "the process of evaluating medical technology (devices, equipment, procedures and drugs) and their uses." It specifies that they use an interdisciplinary approach in assessing safety, efficacy, effectiveness, quality of life and patient use, as well as economic, ethical and social implication and "other effects which may be unintended, indirect or delayed."

According to the Organization for Economic Co-operation and Development (OECD)[112], technology assessment is not a single discipline, but an integrating process across disciplines that helps to build bridges between science economics and policy. Assessments should address whether a new technology is a sustainable solution or the best of all options in a specific healthcare and social context. Health technology assessment is different from many other forms of research in that it produces and communicates information that contributes to the decision and policy making process. To conduct a health technology assessment, three different types of evidence must be gathered and analyzed: scientific (including economic), conceptual, and historic. Usually a variety of organizations are involved in this type of research (government, universities, professional organizations and industry). There may well also be a strong case for involving consumers and various stakeholders in the evaluation of certain forms of technology.[113]

7.5.1 GENETICS AND HEALTH TECHNOLOGY ASSESSMENT

In many cases, genetic testing has moved so quickly from the research bench to the clinical laboratory that there has been little or no opportunity to conduct comprehensive evaluation. Many aspects of genetic tests need to be evaluated if we are to exercise the appropriate caution with new forms of testing – some of the considerations that will require addressing include:

- **Accuracy and reliability:** Tests vary in their sensitivity (the ability to detect mutations or to detect all patients who have or will get the disease) and their specificity (the ability to detect a single or specific target and no others). Inaccurate test results ("false positives" and "false negatives") may do irreparable damage to the lives of many people.

- **Outcomes:** In most forms of pharmaceutical evaluation, outcomes can be fairly easily defined in terms of mortality or morbidity (e.g. number of patients who died, who had a heart attack or who were hospitalized). Genetic testing may require the development of new outcome measures and new ways of assessing the impact of treatment.

- **Utility:** The balance between the benefits and risks associated with a given diagnostic and screening strategy should be considered at the level of both the individual and society. This should include psychosocial impact in the short and long term.

- **Health economics:** The financial cost of testing for the healthcare system, including costs relative to existing treatments and "downstream" or long-term expenses, should be considered. Analyses should focus upon the cost-effectiveness, cost-efficiency, and comparative costs of testing from the point of view of the individual, the healthcare system and the society as a whole.
- **Social impact:** The effects of genetic technology can go beyond mere medical considerations. There is a need to expand the usual evaluation framework in order to accommodate considerations of culture-specific factors, systems analysis, and public attitudes.

Blancquaert et al[114] have suggested that genetic testing should be subjected not simply to basic health technology assessments, but to a two-step implementation process. Before moving from the research setting, an initial evaluation would be conducted, focusing on analytical validity but including data collection on clinical validity and utility.

If the test proved to have analytical validity, it would move into a transitional phase of restricted use (e.g. in tertiary care centres or research-based clinics). The second phase of evaluation would then begin. The second evaluation would continue to build on the data collected during the initial evaluation. Only when and if results of the second evaluation were satisfactory would the test be allowed to move into unrestricted clinical practice.

As well as a two-step evaluation process, Blancquaert et al support independent evaluation of all relevant data, as recommended in 1997 by a National Institutes of Health (NIH) Task Force on Genetic Testing.[115] Tests likely to raise many clinical, ethical or legal issues would require a rigorous and formal evaluation by a multidisciplinary team. Ideally, the Task Force noted, some form of oversight mechanism other than professional self-regulation may be required. While the dilemmas and challenges regarding the funding of new tests will be large, ensuring that appropriate and rigorous assessment and ongoing evaluation are incorporated into new genetics programming and appropriately updated in existing programs will also be required.

There is much already written on genetic technology assessment and effective capacity is already in place in some juridictions from which provinces and territories can potentially benefit.

As has been the case with pharmaceutical assessments, expertise in the assessment and evaluation of genetic tests is currently scattered across a number of jurisdictions, in a number of our research and clinical centres. Building on similar momentum in more co-ordinated pharmaceuticals review, now may be the time for jurisdictions to begin to assemble a common genetic technologies assessment capacity – not to replace the necessary determinations that will have to take place at the level of each jurisdiction (regarding funding this or that new test) but to provide us all collectively with the kind of analysis and perspective that will allow objective decision-making regarding genetic tests. Taking such a step would have the distinct advantage of avoiding the scenario of three or four provincial agencies each undertaking comparable studies on the same test for different jurisdictions.

8. Recommendations

As this report has attempted to outline, all jurisdictions will face a number of challenges in the years ahead as we attempt to incorporate today's research breakthroughs in the realm of genetics into the fabric of healthcare delivery. We face the option as jurisdictions of addressing these social, legal and ethical challenges either independently, one crisis at a time, or collectively, by setting out a roadmap for both cooperation and leadership. Furthermore, the rapid growth of demand for and cost of such emerging technologies, places real challenges on the financial sustainability of the healthcare system.

There is much wisdom, if our jurisdictions are to move forward effectively, in the idea of beginning to develop the basic outlines of a cross-jurisdictional framework on the role of genetics in medicine and society. A framework that would position the patient at the centre and takes into consideration all the legal, ethical, social, economic and implementation issues that will form the basis for the principles of care in genetics.

An interjurisdictional framework has the potential to allow every jurisdiction to draw upon the experience and expertise of others, while still retaining the appropriate levers and supports at the provincial and territorial level. Within any effective framework there will be certain aspects that can only advance fully with the active engagement of the federal government. Provinces and territories simply do not have the constitutional authority nor the currrent fiscal capacity to address some of the key components of an effective framework. Provinces do not possess the levers to change patent law, but all jurisdictions ultimately live with the consequences of decisions made at that level.

Ultimately, any cross-jurisdictional framework must also live within the international agreements and frameworks that Canada adheres to, on trade intellectual property protection, on health and human rights.

The federal government also has a critical role to play in ensuring that the health system is resourced to effectively take advantage of the hope offered by genetics. And what does this mean? It means the resources to train our providers, to recruit the genetic specialists who will undoubtedly be in increasingly short supply, the resources to ensure that new tests and therapies are available, the resources to ensure that appropriate oversight and regulation mechanisms are in place. Whatever the long term impact of genetic breakthroughs will be on the health system, the medium term costs of supporting the transformation will be high and these costs will not easily be found by simply reallocating from other parts of the system.

8.1 INTERJURISDICTIONAL FRAMEWORK

What might the elements of a cross-jurisdictional framework look like? This report is not intended to be at all prescriptive, but merely to provide certain pointers that we, as provinces and territories, might choose to use, both for ourselves and with the federal government as a guide through fairly uncharted terrain.

Possible Action:

Task Health Ministers in conjunction with appropriate colleagues to develop a comprehensive cross-jurisdictional framework on human genetics and healthcare. The framework should be patient centred and take into consideration the social, legal, ethical, financial and health system implementation issues raised by the increasing role of genetic breakthrough in healthcare.

The goal of a comprehensive framework would be to undertake in a co-ordinated manner a wide range of specific actions designed to maximize the ability of the Canadian health system to utlilize the breakthroughs offered by new genetic research in an informed and forward looking manner.

Such a framework should encompass:

a) Co-ordinated and intensified public engagement on the role of genetics in healthcare.

b) Increased opportunities for the education and training of health professionals in genetics and new genetic medicine.

c) Strengthened shared capacity in health technology assessment and health economic analysis for genetics.

d) Developing appropriate shared quality control mechanisms (testing protocols, laboratory and test evaluation mechanisms, appropriate consumer protections).

e) Developing common increased capacity in health human resource planning for genetics and putting in place a shared multi-year plan for genetic expertise in the health system.

f) Developing the common principles to underpin privacy, disability and discrimination protections regarding the use of genetic information particularly in the employment and insurance fields.

g) Examining comprehensive patent reform and reform to the patenting processes for human genetic materials.

h) The establishment of a cross-jurisdictional co-ordinating body to provide assistance and expertise to all jurisdictions (Human Genetics Commission).

i) Putting in place the basis for a co-ordinated shared delivery system for genetic testing across jurisdictions

j) Support for an innovative biotechnology sector through continued examination of international best practices for supporting strength and growth in this sector.

8.2 PUBLIC EDUCATION AND ENGAGEMENT

In our increasingly knowledge-based economy an informed and educated public is a resource for our future development. This is true not only in general terms, but is especially true for our biotechnology sector. In addition to the contribution that public education and engagement bring to the economy, we must equip our society with the means to make informed decisions about its health, and to be able to navigate an increasingly complex series of options that will emerge with predictive testing and other forms of genetic intervention.

The public must be engaged in these issues as we evolve our approaches to genetics. This engagement is a necessary prerequisite to building confidence in biotechnology and educating society about the implications of genetic testing. At a time when public understanding of genetics perhaps does not reflect the sometimes complex interplay of factors that shape individual health, increasing awareness about the relative role of genetics and the multi-level nature of risk is important. Increasing awareness and access to reliable information is essential if Canadians are to make meaningful, thoughtful contributions to decision-making processes not only surrounding their own care, but also about the role of new biotechnology in society.

Education about genetics may be conducted in collaboration with industry and the media, but must be carried out by groups or organizations that are authoritative, respected and objective. Some suggestions include:

- Human Genome Canada (which has a mandate for public education)
- Professional associations
- Governments
- Schools, colleges and universities
- Researchers
- Funding agencies

A number of approaches could be utilized to increase public awareness and understanding of genetics and statistical risk. Tactics that jurisdictions could explore might include: considering school curricula (e.g. adding genetic education at the elementary and secondary level and increasing the amount of genetic education in all relevant post-secondary programs); media relations; advertising; and the development and dissemination of educational materials (internet and paper-based).

In the coming years we will all be faced with the need to engage the public on issues pertaining to genetics and genetic medicine. We need to consider how best to undertake these tasks, how to avoid developing the same resources in different jurisdictions, and how to avoid conveying competing or conflicting messages to the public. A co-ordinated and long term approach to public education not only makes good sense economically: it will likely be more effective in the long term.

Possible Action:

Task Health and Industry/Economic Development Ministers in conjunction with other appropriate colleagues to participate in drawing up an interjurisdictional framework for public education in genetics and biotechnology for future consideration. Such a framework might examine contributions that could be made by a variety of sectors and existing agencies and determine the steps best taken to maximise information sharing and co-ordination.

8.3 PROFESSIONAL EDUCATION

There is an urgent need to educate current and future health professionals about genetics. This will not only allow for greater information to be provided to the public, it will lay the basis for an easier and smoother incorporation of new breakthroughs as they arrive.

This education is perhaps best conducted by the appropriate professional associations, in cooperation with provinces, territories and such bodies as Human Genome Canada and Health Canada. Industry may also be utilized to advance the education of healthcare professionals. Again, the challenge is not only to avoid duplication and the development of multiple and conflicting messages, but also to put in place the basis of a medium to long term framework with which to equip our professionals.

Measures aimed at professional education might also need to go beyond the health professional as caregiver and assess the current capacity and challenges in the area of genetics research and professional education. In this regard provinces and territories may well also benefit from a detailed review of the existing and anticipated educational opportunities and approaches that are available in our post-secondary institutions.

Research ethics boards (REBs) may also require education on genetic issues or greater awareness of existing ethical guidelines and procedures in order to assist them in better meeting the challenges of the genetic era (for instance privacy issues that arise, particularly when genetic information is banked for future unspecified use).

A comprehensive plan involving stakeholders such as professional associations and industry (pharmaceutical and biotechnology companies) needed to ensure that all healthcare professionals receive appropriate and adequate training in genetics and the concept of statistical risk. Professionals who will require this training include all primary care providers in direct communication with patients (e.g. family physicians, nurses and pharmacists), as well as non-genetic medical specialists (e.g. pediatricians, obstetricians, etc.).

Possible Action:

Provincial and territorial Health Ministers through appropriate channels and drawing upon colleagues from other sectors as required could begin undertaking a "census" of where we are now and from this point on, with federal co-operation and financial support and in conjunction with appropriate professional agencies, set out a series of key targets in the area of genetics for improving the training, curriculum, and educational opportunities available to our healthcare workers. The goal would be to develop a multi-year framework for increasing these skills and training opportunities.

8.4 GENETIC TECHNOLOGY ASSESSMENT

Enhanced interjurisdictional co-ordination should be established to share data and broaden the range of evaluation activities conducted on genetic testing. This sort of initiative builds on recent developments in co-ordinated pharmaceutical review. This could potentially take the form of a collaboration between a number of existing research and assessment bodies working in the field. We would envisage this collaboration undertaking timely and comprehensive assessments of new genetic technologies to be made available to all jurisdictions. Jurisdictions could agree to withhold funding of recent interventions or genetic tests until comprehensive technology assessments have been performed. This would allow all jurisdictions to work from the same advanced assessments and avoid "one-off" decisions in one jurisdiction setting precedents for others. Provinces and territories might also benefit from establishing "conditional approval" protocols that might be used to make available a certain forms of testing conditional upon full economic impact, relative cost-benefit, and medical efficacy studies being undertaken.

Economic evidence, cost-benefit assessment and determination of both direct and indirect patient impacts (including psycho-social) should also be integrated into clinical trials (e.g. possibly as a condition of granting a clinical trial). To ensure that these considerations are taken into account, it may be necessary to establish more co-ordinated linkages between any future agency undertaking health technology assessment in genetic technologies with research ethics boards at universities and hospitals across the country already working in this field.

Economic evaluations should be clear in their scope, endpoints, limitation and target audience and include appraisal of where a medical technology is in its life cycle. Reliable and rigorous criteria for health technology assessments, possibly in the form of common formats, should be used nationally and regularly revisited to include new analytical developments. Comprehensive technology assessments will make it easier for the public, professionals and policy makers to make rational and effective decisions on the use and financing of genetic tests relative to other available tests or treatments. Such expanded capacity will help provincial healthcare systems to develop appropriate geographic models of service delivery.[116] It will also play a major role in allowing provinces and territories to counter what may be significant public or provider pressure to make available certain forms of testing prior to adequate evidence being in place. It would also be important to include a surveillance function to ensure longer term monitoring is undertaken subsequent to approval.

Possible Action:

Building on the progress being made by Health Ministers regarding collaborative pharmaceutical assessments, provincial and territorial Health Ministers could be tasked with establishing a workplan, objectives and timeframe for developing optimum current and future collaborative capacity in genetic technology and testing assessment and evaluation. Such a collaborative process should receive at least partial federal funding and be available to all jurisdictions.

Assessment would include economic evidence, relative cost-benefit and medical efficacy studies being conducted both pre and post approval.

Provinces and territories might also wish to task Health Ministers with examining the feasability of "conditional approvals" on certain testing where sufficient evidence is not yet in place to allow a complete determination of the direct and indirect implications of test coverage.

8.5 SERVICE DELIVERY: QUALITY CONTROL

While professional standards and review processes exist across jurisdictions now, additional mechanisms or regulations may well be needed in the future as new testing methodologies and approaches develop, in order to effectively monitor the quality of genetic testing provided across all jurisdictions. Ideally these standards should be common, regularly reviewed and utilized by all jurisdictions. This initiative would strive to put in place protections and appropriate testing protocols that jurisdictions need to develop and maintain. Such a quality control process would include:

- Testing criteria (under what guidelines and to whom should the test be offered?)
- The accuracy and reliability of the test (should the test be offered?)
- The relative benefit of a new test
- The accuracy and reliability of laboratories conducting the test
- Training of test personnel (are they qualified to perform their duties correctly?)
- The testing process (are patients giving informed consent?)
- The availability or anticipated availability of appropriate treatments or interventions
- The degree to which patients are receiving a full package of services (are patients receiving adequate pre- and post-test counselling?)

Possible Action:

Health Ministers could be tasked with establishing a common framework for quality control in genetic testing to be utilized to the extent possible across all jurisdictions. Such a framework which could include testing criteria and standards should build upon existing capacity and expertise and avoid, to the extent possible, duplication and divergent standards.

In addition to genetic testing offered at hospitals and other healthcare facilities, Canadians (and our health system in general) will also be impacted by the possible rise in the availability of at-home tests and potential internet availability of such testing via U.S. labs. Federal standards for approval and review of such at-home tests should be carefully examined and monitored to ensure that they adequately protect Canadians. All jurisdictions would also benefit from being kept informed of progress in this area and the protections in place as new testing evolves.

Possible Action:

Provinces and territories could assess with Health Canada and Industry Canada existing review processes and develop an information sharing capacity regarding new developments in kit and at-home based testing in this regard.

Provinces and territories could also call on the federal government to ensure that direct to consumer marketing of genetic testing should at minimum be clearly circumscribed if not entirely prohibited for certain forms of testing.

8.6 SERVICE DELIVERY: HUMAN RESOURCES

As discussed in Section 6, genetic testing will require the additional training, recruiting and retention of genetic specialists (medical geneticists, genetic counsellors, lab personnel) as well as non-genetic medical specialists and other healthcare professionals (e.g. nurses and pharmacists).

To meet future demand for genetic specialists, we will likely need to increase the number of medical geneticists and genetic counsellors. A comprehensive plan should be made determining the number of specialists required currently, anticipated needs in the following five to seven years, and how these needs might be met. Part of this plan should address the retention of genetic specialists in Canada. The goal should be to ensure that genetic specialists are available in adequate numbers, and in an equitable distribution across the country, to meet the population's needs. The analysis of the supply, distribution, retention and recruitment of specialists should include strategies for achieving the goal, including incentives that may be necessary (e.g. research opportunities).

Possible Action:

Health Ministers could be tasked to use appropriate existing mechanisms such as the Advisory Committee on Health Human Resources (ACHHR), and where appropriate such as the drawing on Education Ministers to undertake a comprehensive review of existing and projected health human resource needs in the field of medical genetics. Health Ministers could be tasked to develop a medium range plan with the goal of providing an adequate and appropriately distributed supply of genetic expertise to residents of all jurisdictions.

Health Ministers might also be tasked with ensuring that ongoing independent capacity is in place to deliver independent quantative analysis on supply, distribution and forecasted requirements of specialized skills in genetics (geneticists, laboratory expertise, counsellors).

8.7 PRIVACY, DISABILITY AND DISCRIMINATION

Consumers, particularly those with genetic diseases, must be represented (e.g. through voluntary associations) when governments and private industry consider the role of genetics in such things as research, insurance, employment law, privacy legislation and family law reform. The concerns of the disabled community about potential uses of genetic information need to be addressed. It is clear that gene technology should be used to assist people with disability and their families, rather than to eliminate diversity.

While there is potential to do much good in the field of genetics, the cautions and fears of eugenics must be taken seriously and inform the lens through which society evaluates the increasing range of testing that will be available. An adequate means of enforcing this principle, whether voluntary or legislative, needs to be developed.

To the extent that existing privacy legislation, for instance the *Federal Personal Information Protection Electronic Documents Act* and provincial health privacy legislation where it exists, does not adequately address issues specific to genetic information, appropriate regulation, perhaps in the form of legislation, is also needed to protect the privacy of individuals and the confidentiality of genetic information. Privacy and confidentiality are becoming increasingly important as the number and types of genetic tests increase. Large databases of genetic information can be created, some of which may exist outside of Canada. Rules for governing access to this information, and for what purposes, must be developed. Canadians need to be assured that data linking and the secondary uses of genetic information are appropriately controlled. Without this protection, confidence in genetic testing will be compromised to the detriment of both healthcare and the biotech sector. Moreover, any regulation must be continuously re-evaluated and modified as the field of genetic testing changes.

The setting of appropriate parameters for the use of genetic information by employers and insurers is a matter of concern to many Canadians. An effort must be made to come to grips with this issue, involving all stakeholders.

Possible Action:

Health Ministers could be tasked in collaboration with appropriate colleagues with developing a set of principles to govern the use of genetic information in the insurance and employment fields. These principles might then be used to either inform appropriate provincial activities or form the basis of legislation or alternate action if such a measure is deemed to be required.

Health ministers might also be tasked with determining appropriate mechanisms to ensure the involvement of people with disabilities in discussions concerning the establishment of future parameters for genetic testing in healthcare.

8.8 PATENT REFORM

As discussed in Section 3, although the principles of patent law have served Canada well, it may be necessary to reform the system to better suit the unique challenges and issues raised by gene patenting. A number of options are available. One approach might be an interjurisdictional body, involving industry, governments, the public, and other stakeholders to decide how to proceed. Whatever the approach, reform is most certainly required in a timely manner.

The goal of any reform should be to uphold the beneficial aspects of patent law (e.g. encouraging research, invention and innovation), while ensuring a better balance between private and public interests with appropriate transparency and rigour.

Possible Action:

Working with governments, industry, patient groups and other stakeholders, the federal government should review the *Patent Act* as it pertains to gene patents. It is important to stress that with the proper balance, a framework can be created that honours Canada's international agreements and protects healthcare institutions and providers while preserving the spur to innovation that the patent system is considered to offer in genetic research. The goal of the review should be modernization of the Act to achieve the objective of a fair and transparent patent review and approval process. This process should recognize the role of gene patents in supporting industry, but put in place appropriate safeguards and protections for healthcare, medical practitioners and researchers. Possible goals to direct the review would include:

a) Ensuring that appropriate protections are put in place to protect healthcare professionals and institutions when using genetic materials in research or the provision of care from legal action or the threat of legal action pertaining to patented genes or DNA sequences. This approach would therefore allow the continued use of different forms of testing (and their patenting) and different interventions each using some or all of the same gene or DNA sequence, but would not allow one gene patent to, in effect, control future subsequent medical use of that gene sequence or portion thereof.

b) Developing new patent office guidelines, procedures and training materials with regards to genetic patents. Clear guidelines must be spelled out providing direction regarding novelty, non-obviousness and utility as they pertain to the issuing of gene patents. Particular attention must be paid in this regard to SNP and EST patenting and include a determination as to whether and under what conditions these sub-gene patents might be granted.

c) Clearly defining the patentable subject matter to exclude broad-based genetic patents covering multiple potential uses and limit patents to clear and well defined specific uses.

d) Clarifying the "experimental use" and "clinical non-commercial use" exceptions in the *Patent Act* to clearly indicate that non-commercial clinical use of patented genetic material and general research use of patented material are excluded.

e) Expanding the "methods of medical treatment" exclusion in the *Patent Act* to put in place explicit liability protections for medical practitioners and institutions for providing publicly funded medical services in the field of genetics including diagnostic genetic services using patented materials.

f) In light of recent developments in human cloning and moves in other jurisdictions to patent stem cell processes pertaining to production of human organs, we would urge the federal government to consider adopting a public ordre or morality clause within the Canadian *Patent Act*. Such a mechanism appropriately modified from the European experience would grant the Commissioner of Patents the ability to reject patents on processes, products and techniques which are deemed to violate Canadian morals and ethics. Such a power does not currently exist.

g) Introducing an opposition period of nine months upon issuance of a new gene patent, based on the current European Patent Office model, to allow interested and affected parties to bring forward reasons for which the content, scope or validity of the patent should be reviewed.

h) Revising the compulsory licensing provisions in the *Patent Act* to cover genetic diagnostic and screening tests in the public healthcare system, thereby allowing the Commissioner the power to grant a compulsory license and to set an appropriate royalty rate after engaging appropriate industry and health sector expertise if required but without prior negotiation with the patentee.

i) Examining the creation of a specialized court to handle appeals of the Commissioner's decisions and to adjudicate in matters of patent validity and infringement.

8.9 INTERJURISDICTIONAL CO-ORDINATING BODY

An interjurisdictional co-ordinating body on genetics, perhaps drawing on the experience of the Human Genetics Commission in the U.K. should be examined. Such a body, building on work already done by Human Genome Canada, could be used formally and informally to draw together provincial and territorial expertise from various sectors to lead the national discussion on the role of genetics in society and medicine. This body could also potentially play a role in co-ordinating and/or monitoring public and professional education undertaken at the provincial and territorial level and function as an expert resource in the implementation of regulatory and procedural frameworks to govern human genetics.

The activities of this interjurisdictional co-ordinating body should be based on a number of fundamental principles established by means of an ongoing dialogue with both stakeholders and the public. This commission should have broad-based representation and act as a resource to all jurisdictions. If established, the body should:

- be based on values and principles which apply across both the public and private sector;
- enable governments to take full advantage of research and development;
- have regard to national and international trends and developments;
- be able to arrive at decisions in a timely and expeditious manner;
- be able to impose or recommend moratoria on activities that may be thought to be ethically or medically unacceptable (e.g. the insurance moratorium in the U.K.)
- be able to examine long term implications for the healthcare system both in terms of service delivery (e.g. personalized medications) and financing sustainability (relationship to emerging technologies).

Possible Action:

Task Health Ministers with developing a draft terms of reference for a possible Genetics Commission, setting out reporting relationships, core goals and objectives and role and responsibility vis-à-vis provincial resources and committees. The Ministers might also be tasked with determining appropriate funding sources for such an initiative, including federal resourcing as an option.

8.10 CO-ORDINATED AVAILABILITY OF TESTING

As genetic testing moves further and further into mainstream medicine, provinces and territories will be faced with increasing pressure to cover the costs of certain tests. In some cases a test may become available which is highly effective or of great predictive or diagnostic value but for which the numbers of individuals requiring the test is so limited that no single jurisdiction will rationally cover the test. Moreover, without national co-ordination we may see that a patchwork of types and forms of testing develop across different jurisdictions, leading to both increased inequities in access and the potential that "orphan" genetic tests will evolve.

One step that could prove valuable in the long term is for jurisdictions to take the first steps to lay the basis for much greater cross-jurisdictional collaboration in the provision of genetic testing services. In jurisdictions where certain forms of testing are not available, protocols might be developed to allow sample testing to be undertaken in another jurisdiction. Another potential benefit to building a collective capacity in genetic testing would be to gradually evolve regional centres specializing in certain forms of testing. This could, in the longer term, have the advantage of providing a broader range of tests to Canadians at a lower cost than the gradual evolution of disconnected systems.

Possible Action:

Task Health Ministers with undertaking the groundwork required to promote a co-ordinated cross-jurisdictional approach to genetic testing. This task could begin with a detailed review of the types and forms of testing that are currently being undertaken by different jurisdictions and the setting out of some key principles and objectives that might form a future framework .

8.11 SUPPORT FOR THE BIOTECHNOLOGY INDUSTRY

The biotechnology sector is a strong and rapidly growing industry and contributes greatly to Canada's economy both in terms of jobs, research and investment. The Canadian genomics industry is the world's second largest biotechnology industry and it is important to continue to support this sector. Canada needs to continue to be a world leader in innovation and research. To this we must continue to provide strong support for the protection of intellectual property within a framework that balances the needs of commerce with the public good.

Finding ways to support the transfer of technology and knowledge into commercial products is of crucial importance to the growth of the biotechnology industry. A supportive technology transfer environment includes both physical commercialization infrastructure, such as research parks and commercialization centres (business incubators), as well as the creation of an entrepreneurial culture to build commercialization receptor capacity.

Biotechnology innovation clusters are key to an internationally competitive biotechnology industry. Biotechnology innovation clusters depend on a sustained, competitive investment in excellent talent, high quality, innovative basic and applied research in a range of sciences, and in the capacity to commercialize the product of that research in a partnership of public-private sector enterprise drawing on multiple levels of government.

A fair, efficient and competitive marketplace is the foundation for investment, innovation, trade and economic growth. As knowledge based firms have considerable latitude in choosing where they do business it is crucial to attract and retain firms while protecting the public and meeting Canada's health and safety standards. Regulatory policies must also be responsive to the rapid changes and advances in technology.

Patents are viewed as the "intellectual" capital of the industry, are the major reward and incentive for innovation, and are necessary for a firm to attract investment capital inside and outside Canada. Canada must adapt its delivery of intellectual property services to the competitive conditions of a global, innovative, fast paced industry.

Possible Action:

Task Industry Ministers to explore priority areas to strengthen the biotechnology sector through a number of innovative means such as:

- **Examining the support to companies in the area of life sciences to encourage research, development and innovation. Such support could include increased funding for research and development, tax and investment incentives.**
- **Continuing the practice of providing special federal funding for the regulation of biotechnology after 2002-2003 to provide resources for the anticipated 500 fold increase in biotechnology applications over the next decade.**
- **Adapting the delivery of intellectual property services provided by the Canadian Intellectual Property Office (CIPO) to provide a sound, predictable intellectual property environment.**
- **Involving the biotechnology industry representatives in discussions to ensure that CIPO provides globally competitive services for biotechnology patenting.**

9 . CONCLUSION

The acceleration of genetic research over the past decade has opened up a new realm of possibilities for human health and wellness, technological innovation and product development flowing from the initial research.

Healthcare in Canada and around the world will eventually be transformed in many ways by the breakthroughs that even a decade ago few of us could have foreseen.

Provinces and territories have much to contribute to preparing society and preparing healthcare to be positioned to draw upon the best of genetic medicine while putting in place the necessary checks and balances which can assist in limiting the risks that undoubtedly come with this terrain.

Building on the tremendous progress that has been made by Canadian researchers in the decoding of the human genome, Canada must now set a goal of not simply housing groundbreaking science, but preparing society to appropriately harness such innovation.

There is much work to be done if provinces and territories are to better understand and equip the public and healthcare providers to address the real challenges that will come with new genetic knowledge and capacity.

This report has sought to provide a series of markers along the way to assist all jurisdictions in coming to terms with their own unique challenges and issues in a manner which allows them to draw upon the experience and expertise of others.

We call on the federal government to play a critical role in supporting this process, in recognizing and acting upon areas of change which are required, but also to give full consideration to the enormity of some of the challenges that healthcare will face as we attempt to re-shape the skills, methods and tools required for the most advanced forms of medicine.

With the right resources and goodwill, provinces and territories have the opportunity to use this critical juncture to carve new paths, to create new models and to draw upon the expertise that exists across all jurisdictions to assist in helping to prepare society and healthcare for the future.

This report is intended to generate discussion and dialogue and to offer some suggested routes for us to take – in the end, the final product will be what jurisdictions choose to make it, the hard work lies ahead.

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Jurisdictional Review*

* This chart does not reflect all of the information available but rather what was currently accessible in English and in most cases on the Internet at the time of this publication. Legislation is subject to change.

Australia	Australian Patent Act states that only human beings, as such, are excluded from patentability. Human organs and derived products (cell lines, genes, DNA sequences) are not covered by this exclusion. Animals are not excluded from patentability either. The Patent Act considers that inventions are a manner of manufacture, which changes the form of a product, therefore isolated and purified proteins are patentable.	Genetic testing for many medical disorders is routine. Neonatal screening for phenylketonuria, hypothryoidism and cystic fibrosis is standard practice, and tissue samples obtained during prenatal screening for cystic fibrosis, along with the corresponding test results, can be stored indefinitely. To qualify for accreditation, laboratories are required to store clinical genetic test results, the corresponding diagnosis and other written information indefinitely after reporting the results to the requesting doctor. If the test is for the purpose of research, the results are stored for a period "in accordance with good research practice".	PRIVACY: Existing legislation relies on a number of Commonwealth, State and Territory legislative instruments, self-regulatory guidelines and common law but there is no specific legislation in any Australian jurisdiction dealing specifically with genetic privacy and non-discrimination. There are a range of sectors in Australia that have no requirements to conform to any privacy or non-discrimination practices (specifically, interactions and transactions in the private sector which is not covered by the Privacy Act. The federal government announced a two-year inquiry into issues of genetic discrimination. Meanwhile, the Human Genetics Society of Australasia and the Australian Consumers' Association have proposed a moratorium on the use of predictive test results by insurers while the inquiry is underway.	The Australian Health Ethics Committee Genetics Working Group developed three documents between 1997-1999 discussing issues surrounding genetics and genetic testing. In August 2001, the Australian Health Ministers' Advisory Council established a working group to assess the implications of the enforcement of gene test patents and develop recommendations.
Austria	Bans the patenting of human organisms and products derived from the human body (ex. genes, DNA sequences, cell lines).	Genetic testing is governed by the Gene Technology Act of 1995 which regulates the contained use of genetically modified organisms, their deliberate release or placing on the market, genetic testing and gene therapy. Gene analysis, as it is defined in the above act, comprises molecular biological investigations of human chromosomes, genes or DNA-segments for the identification of disease-causing mutations. Such examinations are allowed only for research or medical purposes and genetic counselling must be carried out before and after genetic testing, and has to include psychological and social considerations as well.	PRIVACY: It is prohibited for employers and insurance companies to collect, demand, or use data derived from genetic tests. Laboratories where genetic tests for the diagnosis of a predisposition or for the identification of a carrier status of inherited diseases are performed have to be accredited by the competent authority. Genetic tests for the diagnosis of manifested diseases do not require an authorisation but are subject to strict measures for data protection.	Not Known

Belgium	Patent law dated no explicit exclusion of human gene patenting and grants broad use for the patents it grants. Putting European Directive into National legislation is being reviewed (for details see European Union information below).	The Ministry of Social Affairs, Public Health and Environment, is responsible for the approval of new medication, and diagnostics including genetic tests.	PUBLIC DEBATE: In Oct. 2001 Belgium filed a joint opposition (with the Netherlands, Germany, Denmark and the UK) to the EPO against EP 0699754B1 (BRCA 1) a patent granted to Myriad Genetics. The Belgian government put the European Directive on their webpage for public comment and has drafted a law with fundamental differences from the European Directive in regard to the basis of a patentable invention. PRIVACY: In 1992 Belgium adopted a confidentiality law that states "the insurance contract may only be based on the present state of the applicant's health, and not on technical genetic analysis to determine future health".	Consultative committee on bioethics has stressed the significance of the introduction of the principle of informed consent, non-commercialisation of the human body, and non-extensive patent protections. The scientific advisory system, to the Federal and the Regional authorities have not yet released official guidelines on genetic testing or patenting, but have agreed on "protocols" for specific types of genetic tests.
Council of Europe (COE)	"Neither plant, animal nor human derived genes, cells, tissues or organs can be considered as invention and nor be subject o monopolies granted by patents." Calls on European Union member states not to implement directive 98/44/EC, to request the re-negotiation of the directive and support the challenges before the European Court of Justice.	Not Known	DETAILS: The COE calls for: - improved legislation on human gene patenting - a code of conduct for scientists that guarantees freedom of access to genetic resources and benefits - the adoption of a common decsion making principle once its contents have been clarified - the introducing a "bioethics labelling" process for new technologies - the development of an international convention on the use of living matter - the adoption of a supplementary protocol to European Patent Convention that would define the criteria to be used by national jurisdictions in the application of the exclusion on the grounds of morality to the field of human and animal tissue.	Not Known

Czech Republic	Human beings, their organs, as well as all elements derived therefrom, such as cell lines, genes and DNA sequences are not patentable. Methods for surgery, therapy, diagnosis (including stem cell therapy) are also excluded from patentability.	Not Known	AIM: Country aims to adapt its legislation to European standard with a view of joining the European Union.	Not Known
Denmark	Despite the Advisory Council's statement, the Danish Parliament voted narrowly in favour of transposition of the Directive. For details see European Union information below.	Genetic testing is mainly regulated through the legal frameworks that apply to the Danish national health care system as a whole. Prenatal testing and genetic counselling is conducted in a few selected centres. DNA testing is performed in clinical genetic and clinical biochemistry departments mainly housed in university hospitals. Laboratories do not need special accreditation or licensure to practice genetic testing however; laboratories take part in external quality assessment on an individual basis.	PRIVACY: A bill developed by the Minister of Labour and amended by a law reform commission bans the use of genetic tests in connection with employment and insurance. It denies employers or insurance companies the right to ask for or to use any type of genetic tests, and extends to regulate the use of all health information.	The Advisory Council on Ethical Questions issued a statement strongly advising against transposition of the European Directive into national law. The Council considers the patenting of genes as highly unethical and foresees many negative effects for patients in the medical arena.
European Patent Office	The mere discovery of an element of the human body, including the sequence or partial sequence of a gene, cannot constitute a patentable invention. However, an element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.	Not Applicable	Not Applicable	Not Applicable
European Union (EU)	In July 1998 EU (98/44/EC) or the Directive allows human gene patents. The 15 EU members have were supposed to enact the Directive July 30 2000, although only Denmark is in favour of doing so. No other member countries have enacted the directive in their laws. Most countries are in the process of transposing, amending or objecting to it.	Not Applicable	Not Applicable	Not Applicable

Finland	Human beings and human organisms can not be patented or be part of industrial processes. Patents must not be granted for inventions that are contrary to morality, including any product derived from the human body or human embryos. Methods for surgery therapy and diagnosis of animals and humans (including stem cell therapy) cannot be patented. Gene therapy as a therapy, whereas biopharmaceutical products can be considered on par with pharmaceutical products and therefore deemed patentable, as can genetically modified cells, produced via gene therapy technology. Genetic engineering methods applied to humans for purposes other than therapy or diagnosis are not patentable because they are contrary to morality.	Routine genetic testing is carried out in university hospitals and in specialised private laboratories. Although no specific regulations exist on genetic testing, supervision and quality control of both public and private sector laboratories are organised by state authorities. However, a general quality assessment scheme of genetic testing has not yet been developed but the ministry is deciding on possible legislative measures.	Not Known	A Working Party set up by the Ministry of Social Affairs and Health has made recommendations concerning quality assessment, supervision, counselling and use of information in relation to genetic testing.
France	The human body, its elements and its products cannot as such be the object of patents, nor can knowledge relative to the total or partial structure of human genes. Directive 98/44/CE is to replace this test with provisions similar to those contained in the Directive. For details on EU Directive see European Union information above.	Respect for the human body and therapeutic necessity are the only acceptable reason for genetic tests and the individual tested must have consented. In terms of research, "genetic studies of an individual's characteristics can only be carried out for medical purposes or scientific research" and only after consent has been obtained from the individual concerned.	PUBLIC DEBATE: Such a development as 98/44/CE should not be passed without a democratic debate beyond the scientific community and renegotiation of the Directive has been requested. Filed joint opposition (with their Minister of Health and Swiss Colleagues) against the EPO BRCA 1 patent. BIOETHICS LAW: Bioethics Laws established principles that must be respected. They include respect for patient autonomy, respect for medical confidentiality, respect for the privacy and confidentiality of personal data, the use of biological samples, prohibition of using results of genetic tests for purposes other than medical or scientific, procedures of accreditation of materials involved in genetic testing, evaluation of the impact of the tests, education and training of all medical personnel who might be involved in counselling and genetic testing, the need to guarantee correct public information and prohibition of all uses of the information that could produce any form of stigmatisation or unfair discrimination.	Comité Consultatif National d'Ethique states that: - the knowledge of a gene sequence can under no circumstances be considered tantamount to an invented product, and is therefore not patentable - that the government should only implement the Directive with substantial changes (the government reacted by stating that it will not transpose the directive until substantial changes are made at the European level).

Germany	In Oct. 2000 the government adopted a draft implementation law to be passed to the national parliament. The draft includes differences to the Directive. At the same time, the government states that the Directive itself is not adequate and decided to initiate a re-negotiation process on a European level. The government said " …given the latest developments in bio-medical research, the necessary ethical limits to patent law must be protected against efforts to patent parts of the human body, and enforced world-wide…" For details on EU Directive see European Union information above.	There are no specific legal regulations on the application of genetic testing in a narrow sense. There are, however, regulations on the introduction of DNA tests as evidence in criminal courts of justice and within the course of prosecution and crime control. In view of the importance of the issues, however, the federal government has decided to address genetic testing. As a first step, the federal government is considering ratification of the Medical Devices Act.		The Federal Medical Council published comments on the diagnosis of the genetic dispositions and the genome analysis of employees. The German Society for Human Genetics has commented on the issue of genetic testing and made statements on the principles of counselling and education, autonomy and confidentiality.
Greece	Not Known	Genetic testing (biochemical, cytogenetic and molecular) has evolved rapidly and special genetic units/labs were set up in universities, national health system hospitals and private labs throughout the country.	PRIVACY: Insurance companies have agreed to a voluntary code of conduct in that they do not ask for genetic testing prior to insuring patients.	National surveys have been carried out both to measure the public's awareness of prenatal diagnosis and medical geneticists' views on genetic testing.
Hong Kong	Has a half-indigenous patent system, meaning their registry only re-registers UK or EPO or PCT or CN (Chinese Patents). If a patent is granted in either of these countries, then a patent can be granted in Hong Kong provided the procedural formalities are complied with.	Not Known	Not Known	Not Known
Hungary	Not Known	There are no approved guidelines for genetic testing in Hungary. Currently, professionals in university or municipal hospitals are delivering services according to practice based on medical literature, nation-wide and international experience in genetic counselling and discussions at scientific meetings. No agency has jurisdiction over clearing diagnostic services for marketing. However, there is occasional collaboration between service delivery units and industry which supply kits for which licensing has been obtained.	Not Known	An ad hoc committee was named by the Ministry of Health to develop guidelines for genetic screening and testing. For advice concerning professional/ethical/legal aspects of genetic testing, two groups of professionals (all of them qualified researchers or clinicians) are involved: - The Hungarian Society of Human Genetics; - The Medical Genetics Subcommittee of the Hungarian Academy of Sciences.
Ireland	Not Known	No specific guidelines for genetic testing. The responsible Agency is the National Centre for Medical Genetics, which provides advice to the Department of Health and others on matters relating to genetic testing.	Not Known	Ireland has been involved with the UK's Clinical Molecular Genetics Society and the Netherlands in developing laboratory guidelines for molecular genetic testing for specific diseases. The society is now part of the federated British Society for Human Genetics.

Italy	Wants a provision added to the Directive that requires voluntary and informed consent of those from who genetic material is taken for the purposes of a patent. EU Court rejected their attempt to overturn the Directive that allows companies to patent genetic sequences found in plants and animals. For details on EU Directive see European Union information above.	Guidelines strongly discourage the use of over the counter devices for genetic diagnoses. The approval and registration of new genetic tests in under the responsibility of the Ministry of Health.	PUBLIC DEBATE: Voiced "extreme seriousness" of the EPO granting a patent that provides for the isolation and culture of adult and embryonic stem cells, and their modification. Supported the Netherlands challenge to the Directive (with Norway also) before the European Court of Justice (Case C-377/89).	National Bioethics Committee published its opposition to the patentability of human beings and suggested that in the course of transposing the Directive into National Law an interpretation be defined that would rule out all ambiguity regarding the illicit character of human patentability. Italy developed a comprehensive document on genetic testing outlining guidelines for the appropriate use, effectiveness and execution of genetic tests in laboratories with a high standard of quality, guarantees patient autonomy, an adapted psychological and social attendance and pays particular attention to the ethics and confidentiality.
Japan	Human beings cannot be patented, but human organs are not specifically excluded from patentability. Can be inferred that human organs are covered in Japan's Patent Law that bans patents and inventions that are contrary to ordre public or to morality. Products derived from the human body (cell line, genes and DNA sequences) are patentable. Methods for surgery, therapy and diagnosis are methods banned from patentability for humans but not for animals.	The usefulness of clinical genetic analysis is widely accepted but there are no laboratory standards regarding genetic testing.	JAPAN PATENT OFFICE: - in favour of stronger IP rights for biotechnology - aware of the problems that may arise from patenting the human genome	Council Committee of Ethics of the Japan Society of Human Genetics revised previous guidelines for genetic testing and counselling. Guidelines apply to members of the Japan Society of Human Genetics and include issues such as autonomy, informed consent, counselling, confidentiality and access, communication of results and accreditation.
New Zealand	The NZ government has agreed as of November 2001 to amend the Patents Act of 1953 and to consider adding a specific exclusion to the patentability of individual genes.	Has a strong and direct interest in gene testing. Much of the testing for New Zealand's genetic services is carried out in Australia.	PRIVACY: The basic tenets of confidentiality of individual health information have also been long acknowledged in privacy law. The Privacy Commissioner issued the Health Information Privacy Code that protects "health information" held by a health agency from unauthorised disclosure and stated that genetic information should be considered "health information" until more is known about the context in which genetic information is held, obtained, used and disclosed. There is general agreement that many of the basic provisions of the Act and Code will control collection, storage and use of genetic information. Protection against the use of genetic information by third parties to discriminate against an individual may exist under the Human Rights Act 1993, that prohibits discrimination on the grounds of "disability", including loss or abnormality of ... physiological or anatomical structure or function.	Representative on the Australian Health Ministers' Advisory Council assessing the implications of the enforcement of gene test patents and to recommend an approach to dealing with this issue. National Advisory Committee on Core Health and Disability Support Services published a detailed report that discusses priorities for service provision in three main areas: 1) Clinical genetic services for diagnosis, counselling, education, information and treatment; 2) Laboratory services to identify affected individuals and people at risk of developing genetic diseases; and 3) Screening services such as antenatal screening to detect foetal abnormalities or new-born screening to identify conditions which may be treated or those which are likely to recur in future pregnancies.

Norway	European Union court rejected their attempt to overturn the Directive allowing companies to patent genetic sequences found in plants and animals. For details on EU Directive see European Union information above.	There has been separate legislation on genetic testing since 1994 that regulates gene therapy and reproductive technology. In it: - a distinction is made between testing before and after birth - very few restrictions are set on access to genetic testing for individuals who are already ill and for predictive testing in healthy individuals and carrier testing - written consent is required - genetic counselling should be given before and after the testing - in relation to another person, it is forbidden to request, receive, retain or make use of information that derives from genetic testing and it is also prohibited to ask whether a genetic test has been performed.	PUBLIC DEBATE: Supported the Netherlands challenge to the Directive (with Italy also) before the European Court of Justice (Case C-377/89).	The Norwegian Board of Health appointed an advisory board. The Board has recently established a Working Group on genetic testing after birth. In addition, the Biotechnology Advisory Board is consulted on matters relating to the ethics of genetic testing.
Republic of Korea	Neither human beings nor their organs can be patented. Products derived from the human body (cell lines, DNA, genes) can be patented. No provision of the law excluded the patentability of animals. Korean legislation takes into account the ways in which products are obtained; products which can only be obtained via methods requiring the use of the human body or its parts cannot be patented. Issues of public order, morality and public health provide grounds for exclusion.	Not Known	Not Known	Not Known
Sweden	Patents on genes and genetic tests are acceptable if they meet basic patentability criteria: novel, inventive step, industrial applicability and reproducibility. Sweden is currently implementing the biotech-directive (98/44/EC). For details on EU Directive see European Union information above.	In terms of research, granting permits for genetic tests takes into account whether the study has a clear, medically justified aim and whether the genetic information collected will be effectively safeguarded. Participation in any study is voluntary, and written consent must be obtained from the participant.	PRIVACY: Genetic information about an individual's susceptibility to a certain disease is only to be used for medical purposes. The Association of Swedish Insurers released a statement whereby "the insurer will not inquire about results from genetic testing or take into consideration such results when assessing risks below SEK 250 000".	Not Known

Switzerland	Human beings are not patentable, whereas products of human origin, including elements isolated from the human body or otherwise produced using technological processes may constitute patentable inventions.	Not Known	PUBLIC DEBATE: Switzerland joint opposition (with the French Minister of Health and their French Colleagues) against the EPO BRCA 1 patent. GENE MODIFICATION: Methods involving genetic modification of humans are prohibited by the Swiss Constitution.	Not Known
Taiwan	Bans patentability for inventions contrary to ordre public, morality and health. Nothing specifically written on human gene patents however, there is a research exemption since protected "product" (genetic resources) may be used free of charge and without restrictions by scientists wanting to create new varieties.	Not Known	Not Known	Not Known
Turkey	Unknown	With a high incidence of autosomal recessive diseases therefore genetic testing is becoming very important in the health care system. Genetic testing is undertaken by molecular genetic units mostly in university hospitals and in a limited number of private laboratories. All private and public laboratories need to be licensed by the health ministry in order to carry out genetic testing. The Ministry of Health has jurisdiction over the import permits for diagnostics tests and devices. Most molecular biological kits and diagnostics are imported.	Not Known	The Turkish Association for Medical Genetics organizes quality control and assurance programmes. In 2000 a meeting was organised to discuss quality assurance programmes for genetic testing.

The Netherlands	Wants a provision added to Directive that requires voluntary and informed consent of those from who genetic material is taken for the purposes of a patent. European Union court rejected their attempt to overturn the European Union law allowing companies to patent genetic sequences found in plants and animals. For details on EU Directive see European Union information above.	Guidelines on clinical genetic testing and counselling apply to "postnatal and prenatal chromosome, biochemical and DNA testing, the clinical removal of foetal material, advanced ultrasound scanning for foetal abnormalities and complex genetic counselling". The regulations are designed to assure the quality and continuity of the procedures in question, which are regarded as a form of medical care.	PUBLIC DEBATE: Has challenged the Directive (with Italy and Norway) before the European Court of Justice (Case C-377/89). The Dutch Parliament is unwilling to transpose the Directive without major changes. They had argued that plants, animals and parts of the human body should not be patented themselves, that only biotechnological processes should be patented. [The court said there were sufficient ethical safeguards in the law such as a ban on patenting the processes to make human clones.] PRIVACY: The Medical Examination Act prohibits insurers from requiring medical tests that could indicate that the applicant might be suffering from a severe, incurable disease.	Standing Committee on Genetics published a report on clinical genetic testing and counselling. Scientific advances in the field of genetics raises such questions as how people should be informed about genetic abnormalities. The opportunities and problems surrounding gene therapy (topic that have also been subject of an advisory committee report).
U.K.	Legislation makes no explicit reference to the patentability of human beings or their organs, but this is excluded on the grounds that it is contrary to morality and does not have industrial application. Derived elements, such as cell lines, genes and DNA sequences are patentable. Animals are also patentable.			Nuffield Council on Bioethics called for the establishment of a central co-ordinating body to monitor genetic screening programmes. The conclusions of the report have been widely endorsed. The Advisory Committee on Genetic Testing and the Human Genetics Advisory Commission have advised Health Ministers on developments in genetic testing on the ethical, social and scientific aspects of testing and on the requirements to be met by suppliers of genetic testing services. They also considered the use, or potential use, of tests both for clinical practice and for those supplied directly to the public. The Human Genetics Commission analyses developments in human genetics to advise ministers on their impact on human health and healthcare, their social, ethical, legal and economic implications while taking account of legal and other differences between England, Scotland, Wales and Northern Ireland, and of the status of devolved and non-devolved matters. Genetics and Insurance Committee evaluates specific genetic tests for their application to particular conditions and their reliability and relevance to particular types of insurance. Gene Therapy Advisory Committee advises health ministers on developments in gene therapy research and their implications. It reviews and if appropriate approves individual protocols for gene therapy research.

U.S.A.	US Patent and Trademark Office (USPTO) regulated by US Code 35 (1052, amended 1999) specifically provided for the patentability of biotechnological processes. USPTO grants extensive intellectual property rights with exemptions granted only for "laws of nature, physical phenomena, or abstract ideas." USPTO grants patents for ESTs and SNPs	Gene testing is currently underway and demand is growing exponentially.	PRIVACY: Health Insurance Portability and Accountability Act prohibits health insurance discrimination based on genetic information. The US Department of Health and Human Services set standards for privacy of individually identifiable health information. The Office of the President issued an executive order banning genetic discrimination in the federal workplace. The Americans with Disabilities Act prohibits genetic discrimination in the workplace by the Equal Employment Opportunity Commission. PUBLIC DEBATE: Some scientists argued that making ESTs and SNPs patentable shows excessive use of the USPTO and that such patents may seriously jeopardise the patenting of whole genes. The National Academies of Science have voiced concerns that the USPTO was granting patents for "DNA fragments which are easy to find and not biologically significant." The National Institutes of Health took a position similar.	At least three advisory groups or committees are currently in place to provide advice on genetic testing. 1) U.S. National Institutes of Health - Department of Energy Working Group on Ethical, Legal and Social Implications of Human Genome Research. 2) The U.S. Secretary of Health and Human Services chartered the Secretary's Advisory Committee on Genetic Testing to help address the range of emerging policy issues raised by genetic testing. 3) The Clinical Laboratory Improvement Amendments Committee, which meets on an ad hoc basis, provides advice to the Centers for Disease Control on laboratory genetic testing issues. The Food and Drug Administration is in the process of chartering an advisory panel to provide input on development of classifications, guidance, and policies for its oversight of devices to be used in genetic testing laboratories and to assist with product reviews when needed.

Medical Professional Organization Positions on Gene Patenting

American Medical Association (AMA)

The AMA supports the concept of gene patents under certain conditions and plans to monitor of the impact of gene patenting and licensing agreements on access to relevant medical care. AMA supports gene patents if:

1) the inventor has demonstrated a practical, real world, specific and substantial use (credible utility) for the sequence;

2) equitable access to licenses or sublicenses are available with reasonable royalty fees;

3) it encourages further discussion on what 'credible utility' should refer to within the field of biotechnology.

American College of Medical Genetics (ACMG)

Stating that genes and gene mutations are naturally occurring substances that should not be patented, ACMG's position is that gene patents should be granted only if:

1) patents on genes with clinical implications are broadly licensed; and

2) licensing agreements do not limit access through excessive royalties and/or unreasonable terms.

British Medical Association (BMA)

The BMA calls for tighter European guidelines on the patenting of human genes. Their position comes from the belief that current gene patent guidelines give too much control to commercial firms and can also give a "financial lock" on future medical conditions.

Canadian College of Medical Geneticists (CCMG)

CCMG is concerned that unrestricted enforcement of gene patents would permit commercial monopolies that would markedly increase costs to the health care system and negatively impact availability, utilization and uptake of services.

Canadian Medical Association (CMA)

CMA has not yet stated their position on the patenting of human genes.

Royal College of Pathologists of Australasia (RCPA)

RCPA considers genes and their mutations as naturally occurring substances that should not be patented. Further, RCPA states that gene patenting creates negative consequences with respect to access and cost of testing, reduction in peer review, conflicts of interest, restriction of further research activity and loss of opportunity for training of laboratory scientists, geneticists, pathologists and physicians.

World Medical Association (WMA)

WMA has called on national medical associations to approach their governments and oppose the patenting of the human genome. Their reasoning is that patenting the human genome has great potential to place "limitation on the availability of new treatments for patients" and cause "restrictions on the transfer of knowledge."

Predictive Tests and Healthcare Costs:

FINAL REPORT
PREPARED FOR THE ONTARIO MINISTRY OF HEALTH AND LONG TERM CARE

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Predictive Tests and Healthcare Costs

Executive Summary

Genetic testing has long been part of Canada's health system, but the scope of genetic testing is growing into new areas. Whereas traditional tests predominantly foretell the health of future generations, new tests increasingly tell individuals about their own health and risks. And whereas traditional tests have focused on rare, single-gene, genetically determined disorders, new tests target common, complex, and multifactorial diseases in which genetics plays only a part. These trends lead to unprecedented clinical and popular interest in genetic tests, and the expanded use of testing will affect both population health and health care costs. Whether the net effects will be positive or negative is a matter of heated debate. Early policy decisions about how tests will be disseminated, provided, and funded will greatly influence the cost and other impacts of new predictive genetic tests.

This report examines the potential effect of new predictive genetic test services on health care costs. We offer a general framework that identifies key factors determining the cost impact of a predictive genetic test service and suggests how the choices of health system decision makers influence costs. We also present cost analyses of four specific predictive genetic tests. The report focuses solely on financial cost implications from the formal health care system's point of view, and does not address the very important questions of impacts on health, wellbeing, productivity, societal costs, or informal care giving

The cost impact of a predictive genetic test depends on, among other things, characteristics of the test, the scope of its application, and the changes in health care utilization (disease surveillance, prevention, and treatment) induced by the test result. For many tests, the cost of performing the test itself makes up only a small proportion of the total health care costs that follow from its use.

Predictive genetic tests cannot be meaningfully analyzed as one monolithic health technology. We distinguish three types of predictive genetic tests on the basis of their predictive power and the genetic nature of the health conditions they address. Full Penetrance tests are used to predict diseases in which a genetic mutation causes the disease in all individuals with the condition. That is, those with the mutation will get the disease, and virtually all those with the disease have the mutation. Such tests are highly predictive and such conditions are rare (e.g., Huntington's disease). Predisposition tests are highly, but not fully, predictive for relatively rare conditions with a strong genetic component (e.g., familial breast cancer). A substantial proportion of individuals with the genetic mutation will develop the condition while those without the marker will not. Risk factor tests have much lower predictive power, and are used to predict common, multifactorial conditions in which genetics plays a limited role (e.g., heart disease). While individuals with the genetic mutation are at increased risk for the health condition, most will not succumb to it, while many without the genetic mutation will.

The effective predictive power of a genetic test depends upon both the diagnostic features of the test itself (how well can it distinguish those with and without the genetic mutation), the relation between the genetic mutation and the likelihood of developing the disease, and the epidemiology of the population in which it is applied, including the underlying prevalence of the genetic mutation and the disease of concern.

Even an excellent, highly predictive test will generate a very high proportion of false results (e.g., the majority of "positives" being false) if applied to a low risk population. Full penetrance and predisposition tests are of least concern in this respect as they have natural target populations: individuals identified by the clinical hallmarks of the condition or by biological relationship to an individual already identified as having the condition. Risk factor tests, in contrast, may apply to the general population for screening purposes, and therefore are more susceptible to generating false and clinically misleading results. The actual target populations for a genetic test will depend on such issues as system capacity, patient and clinician demand, options for clinical management (i.e., surveillance, prevention and treatment), and gatekeeping structures (e.g., referral protocols, designated providers, direct consumer marketing).

The effect of the genetic testing service on health care costs depends on the pattern by which the test classifies tested individuals as "positive" (has genetic mutation) and negative (does not have genetic mutation), and how individuals with each of these results changes their health care consumption patterns. To estimate the cost impact of a test, therefore, one must model what individuals do based on the new genetic information they get from the test, as well as what they would have done without it. Four basic categories of health care expenditure that might change include: (1) cost of identifying those who will develop the disease; (2) the cost of surveillance among those thought to be at high risk; (3) the cost of preventive care; and (4) the cost of treatment if the disease occurs. The effects on each of these types of costs depends not only on the test itself, but also on individual and provider behaviour, the current state-of-the-art of clinical practice with respect to non-genetic screening, surveillance, prevention, and treatment technologies. New developments in any of these three areas will affect clinical options, behavioural choices, and their consequent costs. If a genetic test replaces the use of a more expensive non-genetic test, then the genetic test could reduce the overall costs of case-finding; if, however, it is use in addition to existing case-finding services, it will be cost increasing. Similarly, if the current practice is to conduct disease surveillance on high risk individuals and/or for such individuals to utilize preventive services, if the test allows us to definitively determine that a person is not at risk, it could again reduce health care costs. In contrast, if a test, especially one that results in a large number of false positives, induces large number of people to unnecessarily utilize surveillance or preventive services, then the test will be cost increasing. Finally, predictive genetic tests could reduce treatment costs if it encourages truly high risk individuals to utilize effective surveillance or preventive services that reduce the occurrence or severity of disease.

Full penetrance tests will, on average, have the smallest impact on aggregate costs because the diseases with which they are associated are rare and because they are easiest to target on high-risk individuals. Risk factor tests likely have the largest variance in their impact on aggregate costs because they have the potential to affect large sections of the population.

We present cost analyses for four specific predictive genetic tests: Familial Adenomatous Polyposis (FAP), Herditary Nonpolyposis Colorectal Cancer (HNPCC), Hereditary Hemochromatosis (HH), and APOE testing for alzheimer's disease. FAP is a full penetrance test, HNPCC and HH are predisposition tests, and APOE is a risk factor test. The cost analyses for HNPCC and HH are based only on the published literature; the cost analyses for FAP and APOE combine evidence from the published literature and an original costing exercise. The analysis indicates that on net, the test for FAP would reduce costs (the savings from reduced surveillance costs exceed the cost of the test) by $1369 per person tested when testing is restricted to family members of individuals diagnosed with the disease. Because the disease is so rare, a test program would generate total savings of approximately $200,000 in Ontario. There is insufficient information to judge the cost impact of genetic testing for HNPCC. Based on figures from the literature, a targeted screening program for HH would generate savings of approximately $1 per person tested, leading to total savings of approximately $300,000 for Ontario. However, and untargeted screening program may generate increased costs up to $60 million. Finally, on balance, a program of APOE testing targeted at high-risk individuals already diagnosed with mild cognitive impairment, is estimated to increase health care costs by $579 per person tested. An estimate of the total cost impact, which is admittedly only a ballpark figure, is that the aggregate cost impact in Ontario for a program similar to the one analyzed would increase costs by $10 to $20 million. It must be emphasized that the above figures should not be interpreted as predictions of what would happen, but are meant only as rough estimates to indicate the order of magnitude of the cost impacts of the tests analyzed.

A range of considerations that cannot be included in the analyses of individual tests that will influence the ultimate impact of the development of predictive genetic tests on health care costs. We have little knowledge of how consumers and providers will respond to the information generated by the tests. Yet, their responses will be central to the ultimate cost impact. And their responses may well be influenced by the fact that, unlike non-genetic screening, for-profit corporations now hold exclusive patents on many genetic testing technologies. They have incentive to push for broad adoption of such tests and may pursue aggressive marketing practices to advance their economic interests. This may particularly be the case when organizations sell goods and services complementary to the genetic test (a practice already seen for non-genetic tests such as bone-densitometry and serum lipid testing).

Coverage decisions for predictive genetic tests will have to be made on a case-by-case basis. Three basic coverage options exist: (1) no public coverage with a private market allowed; (2) unrestricted public coverage; and (3) criteria-based public coverage. The first option opens the market for such tests to more market-oriented dynamics and, while it does save the public funder the cost of the test itself, it does not avoid the other health care costs, most of which will be publicly financed. In the end, the costs savings would be small and the public funder has lesser ability to regulate use. The second case ensures broader access but will have the largest cost impact on the public funder. The third option, criteria-based public coverage, provides access to those in need while giving public funders the most levers to limit use to situations where the tests are most likely to produce benefits and avoid broad, inappropriate uptake that would generate large costs to the public system.

The Bigger Picture

As illustrated in the preceding sections, estimating the economic impact of genetic testing services is far from straightforward. Part of the complexity stems from the complicated and inexact relationship between genetics and health (Evans, Skrzynia et al. 2001). Further challenges come from uncertainty regarding how genetic information will influence patients, providers, and other stakeholders. Neither the simplified micro-assessments of individual tests previously conducted in the economic literature, nor the grand promises of enthusiastic promoters of genetic technology address many of the important issues at stake. A balanced assessment of genetic testing services must consider not only the technology, but also that there are important, albeit difficult to quantify, psychological costs associated with genetic testing; that individuals will, upon testing positive for a gene-related risk, seek to reduce their susceptibility, regardless of whether appropriate health care is available; that the genetic testing industry is—now more than ever—profit driven; and that it is difficult to evaluate the long-term impacts of preventative treatments for gene-related risks. Finally, from the perspective of the public provider of health care, coverage decisions must be considered with emphasis on both access and appropriateness of use.

Imperfections in test sensitivity and test specificity lead to false negatives and false positives that must be accounted for in any screening or diagnostic service. In the case of genetic testing, however, the complex and inexact relationship between genetics and health, as well as the potentially long period between genetic testing and illness onset, exacerbate these issues. Pre-symptomatic genetic tests that predict illness with certainty are rare. Most nascent genetic tests aim to identify populations at risk of illness. Some people with genetic susceptibility will not develop the illness of concern, while some "normal" genotypes will. As discussed above, the costs and consequences of these dynamics must be considered.

A primary purpose of predictive genetic testing is to alter the behaviour of persons identified at risk of future illness. Knowledge of a genetic susceptibility to illness focuses attention and intention on prevention. Patients and practitioners may be prone to action for fear of the regret (or legal liability) that might ensue should nothing be done. The impulse to respond may, in some cases, exceed evidence of preventative or treatment effectiveness. However, it is also possible that patients labeled at risk of illness will experience a sense of fatalism, possibly reducing (or at least not encouraging) preventative behaviours (Marteau and Lerman 2001). These dynamics are not new, however. They are similar to the impacts from non-genetic screening programs. The response of individuals to information about health risk depends on the test, context, and perceived efficacy of preventative behaviours (Marteau and Lerman 2001).

In addition to induced preventative behaviours (or lack thereof), susceptibility information can also have an impact on health status. Direct health impacts of health risk information have been observed in non-genetic screening programs (Peckham and Dezateux 1998) (Stewart-Brown and Farmer 1997). In some settings, those identified at risk of certain illnesses through non-genetic screening programs (e.g., hypertension and cholesterol screening) have been shown to have lower self-reported health status and/or higher all-cause morbidity and mortality (Peckham and Dezateux 1998) (Stewart-Brown and Farmer 1997). This form of self-fulfilling prophecy when labeling populations at risk of future ill health may carry over to genetic screening if patients interpret risk information in a similar manner. Though difficult to predict, these dynamics must be weighted against the benefits to those who ultimately gain from screening and subsequent treatment.

One determinant of behavioural and health responses will be how the benefits and costs of testing, and ultimately of treatments, are communicated to the public, and to practitioners. Unlike most non-genetic screening services, for-profit corporations now hold exclusive patents on the many genetic testing technologies. This affects not only the cost of the tests themselves, but also the way that genetic testing is portrayed to providers, patients, and the general public. Patents concentrate the economic interests associated with specific technologies by conferring a temporary monopoly upon the inventor. The reward for invention is determined by the price the market will bear for the technology, and the extent of its adoption, giving an economic incentive to push for rapid and broad application of new, patented technologies. As the breadth of genetic testing services expands to include the promotion of tests for common disorders, the potential demand induced by marketing may outpace our capacity to offer genetic counseling necessary for informed consent (Collins 1999). Moreover, some genetic testing services may be marketed before effective preventative treatments are available. Some tests may even be promoted before much can be done to manage the risks they identify.

Where preventative therapies currently exist, genetic testing services may also be promoted by those selling these goods and service that could be seen as complementary to the genetic test. This has occurred in the case of non-genetic screening programs—e.g., bone-densitometry, serum lipid testing—where specific companies selling drugs to manage those risk factors have financial interest in promoting the screening programs themselves. Current models of pharmacological disease management may evolve along with genetic testing, offering products and services to the "market segment" created by those determined to be at greater than standard risk of given illnesses. In many cases, the cost of complementary treatments will exceed (possibly by far) the cost of the genetic testing itself.

The evaluation of preventative responses to genetic testing services (including pharmacological disease management responses) is critical for determining the overall cost of genetic testing service. This task will not be easy. Clinical benefits from preventative products and services consumed upon the identification of genetic susceptibility to many illnesses will not be observable for many years, in some case decades. As the time-line involved becomes longer, the savings or health improvements required to justify ongoing costs of prevention must increase. Determining the end-state savings from prevention will be difficult because it is uncertain whether what is known about the expected benefits of existing treatment modalities can be applied to treatments given to those at genetic risk of illnesses. For example, treatments used to manage biological factors associated with the risk of later illness—such as blood pressure or cholesterol levels–have historically been approved based on changes in the biological marker as a surrogate of their impact on long-term health. It is yet unknown whether such surrogates will apply to risks of a genetic origin. The costs of treating susceptible populations with such therapies will, nevertheless, add up over time as we wait for evidence of long-term efficacy.

The importance of the treatment or preventative therapy that follows genetic testing services highlights a consideration regarding the funding of genetic testing services themselves. The costs of genetic testing itself may be outweighed by the costs related to services induced by the test results. Consequently, whether or not a test is provided publicly, much of the cost associated with goods and services complementary to the test will be born by the public system.

Coverage decisions will of course have to be made on a case-by-case basis. One can envision three scenarios for the coverage of a given predictive genetic test: (1) no public coverage; (2) unrestricted public coverage, or (3) criteria-based public coverage. In all cases, the publicly financed health care system (so long as it remains reasonably comprehensive) will end up paying for many services complementary to the genetic test, including pre- and post- test primary care, induced medical or surgical treatments, or long-term preventative therapy (possibly including drug costs, depending on eligibility). Caulfield and colleagues offer a number of criteria to determine whether the tests themselves are appropriate for public funding: these include whether the test is morally appropriate, safe, accurate, and clinically useful (Caulfield, Burgess et al. 2001). When tests are available exclusively through the private sector, willingness and ability to pay for tests becomes the mechanism of test rationing. This allocation method may not be consistent with allocation according to need. In cases where the test could be deemed medically necessary, but the patient is unable to afford the test, this will violate the spirit of the Canada Health Act. Of course, when a test is immoral, unsafe, inaccurate, or clinically useless, private payment for tests does not violate principals of Canada's health care system. Private payment for such dubious tests may still cost the public system in terms of complementary services. In general, leaving predictive genetic testing services to the private sector will save the publicly funded system the cost of the tests themselves, but if forsakes the ability to regulate use.

Unrestricted access to tests through the public system will alleviate financial barriers to access, but may result in excessive test use. Many tests currently available prove to be most appropriate and cost-effective when applied to limited populations–e.g., those with a familial susceptibility to a given illness. If demand for tests induced by promotion of the testing technologies extends beyond the realm of targeted populations, costs will increase without necessarily being accompanied by commensurate savings or health improvements.

Consequently, the wisest policy in many circumstances may be to provide public coverage for the test along with test service programs that target delivery at high-risk populations. That is, public coverage may give public funders the most levers to limit use to situations where the tests are most likely to product benefits and to avoid broad, inappropriate uptake that would generate large costs to the public system. Criteria-based public coverage for many genetic tests may ensure access and efficiency. Unnecessary use of tests will only be avoided, however, if denial of public coverage on reasoned and needs-based grounds sends a signal to patients that dissuades them from seeking the test through the private market–complementary costs of which would ultimately be borne by the public system.

Conclusions

The above analyses highlight the difficulties encountered in predicting the cost impacts of predictive genetic tests on health care costs. As with most health care services, no general a priori statements can be made regarding the cost impact. The effect of each test depends on the specific features of the test, how it is used, and the current practice with respect to the condition associated with the genetic test. Further, even a "good test" that has the potential to be cost reducing when targeted at high-risk populations could generate large increases in costs if applied more widely. Many other tests will unquestionably be cost increasing (and may also generate corresponding gains in health and well-being if wisely used). A couple of key points emerge from this analysis.

Full penetrance tests, which test for rate diseases and can be well-targeted, will have the smallest impact on health care costs. Predisposition tests, if well-targeted will also likely have small costs impact. However, because the test for specific heritable forms of more common diseases, there is some possibility that they may be applied more broadly than in appropriate, generating large cost impacts. Risk factor tests will likely have the largest impact on costs, and they pose the greatest challenge for limiting use to appropriate conditions.

The cost impact of predictive genetic testing itself is only one component of overall system costs. In many cases, it is a minor cost compared to cost for surveillance, prevention or treatment. Hence, although it is appropriate to ensure that the tests can be delivered at the lowest cost possible, attention also needs to be focused on other cost effects of introducing a predictive genetic test service. Hence, even if the test is offered only privately, much of the cost impact may arise in the publicly financed components of the system. Coverage policies need to take into account the overall relation between where the costs arise and the ability of the public funder to control access to tests that generate public-sector costs even when the test is privately financed.

Finally, a number of key parameters that influence the impact of predictive genetic tests on overall system costs are under the control of health system decision makers at various levels of the system (e.g., the design of the testing service and how well the test is targeted). Hence, the impact of predictive genetic tests is not an immutable force. Wise policy choices can ensure that savings are realized were possible and, where cost increasing under all circumstance to ensure that the most value is obtained for the resources devoted to testing.

Selected Glossary

Base Pairs

Are found in nucleotides (ATCG) and form the basis of genetic codes. One base lies on one side of a strand of a DNA double helix, and one on the other. The number of base pairs in a DNA segment are often used to measure its length.

Bioinformatics

The development of new tools for the analysis of genomic and molecular biological data.

Biotechnology

A set of biological techniques developed through basic research and now applied to research and product development.

Cell

The basic unit of any living organism that contains a complete copy of the organism's genome.

Cytogenetics

The study of the structure, function and abnormalities of human chromosomes.

DNA (deoxyribonucleic acid)

The chemical inside the nucleus of a cell that carries the genetic instructions for making living organisms.

DNA Marker

A segment of DNA with an identifiable physical location on a chromosome and whose inheritance can be followed.

DNA Sequencing

Methods of determining the exact order of the base pairs in a segment of DNA.

EST (expressed sequence tags)

Short sequence of DNA that has a single occurrence in the human genome and whose location and base sequence are known. ESTs are useful for localizing and orienting the mapping and sequence data reported from many different laboratories and serve as landmarks on the developing physical map of the human genome.

Gene

The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making specific proteins.

Gene Mapping

Determining the relative positions of genes on a chromosome and the distance between them.

Gene Therapy

Experimental treatment of a genetic disorder by replacing, supplementing or manipulating the expression of abnormal genes with normally functioning genes.

Gene Transfer

Incorporation of new DNA into and organism's cells, usually by a vector such as a modified virus. Used in gene therapy.

Genetic Counselling

A process comprised of: evaluation to confirm, diagnose, or exclude a genetic condition, malformation syndrome, or isolated birth defect; discussion of natural history and the role of heredity; identification of medical management issues; calculation and communication of genetic risks; and provision of or referral for psychosocial support.

Genetic Predisposition

Increased susceptibility to a particular disease due to the presence of one or more gene mutations, and/or a combination of alleles, not necessarily abnormal, that is associated with an increased risk for the disease, and/or a family history that indicates an increased risk for the disease.

Germline Cell

The cell line from which egg or sperm cells (gametes) are derived.

Genotype

The genetic constitution of an organism or cell.

Human Genome

The complete DNA sequence, containing all genetic information and supporting proteins, in the chromosomes of an individual.

Human Genome Project

An international research project to map each human gene and to completely sequence human DNA.

Inherited

Transmitted through genes from parents to offspring.

Intellectual Property Rights

Patents, copyrights, and trademarks.

Informed Consent

The permission of an individual to proceed with a specific test or procedure, with an understanding of the risks, benefits, limitations and potential implications of the procedure itself and its results.

Mutation

A permanent structural alteration in DNA.

Monogenic Disorders

A disorder controlled by or associated with a single gene.

Mendelian Disorder

Manner in which genes and traits are passed from parents to children. Examples of Mendelian inheritance include dominant, recessive and sex-linked genes.

Multigenic Factors

Genetic disorders resulting from the combined action of alleles of more than one gene. Although such disorders are inherited, they depend on the simultaneous presence of several alleles; thus the hereditary patterns are usually more complex than those of monogenic disorders.

Non-Coding DNA

The strand of DNA that does not carry the information necessary to make a protein.

Patent

When applied to genetics, the government regulations or requirements conferring the right or title to an individual or organization to genes under certain criteria.

Pharmacogentics

The study of how genes affect the way people respond to medicines.

Pharmacogenomics

The study of the interaction of an individual's genetic makeup and response to a drug.

Polymorphisms

Natural variations in a gene, DNA sequence, or chromosome that have no adverse effects on the individual.

Proteomics

Systematic analysis of protein expression of normal and diseased tissues that involves the separation, identification and characterization of all of the proteins in an organism.

SNP (Single Nucleotide Polymorphisms)

Common, but minute, variations that occur in human DNA at a frequency of one every 1,000 bases.

Somatic Cell

Any cell in the body except germline cells and their precursors.

Stem Cell

Cells that can replicate indefinitely and can differentiate into other cells.

Predictive Testing

Testing offered to asymptomatic individuals with a family history of a genetic disorder and a potential risk to eventually develop the disorder.